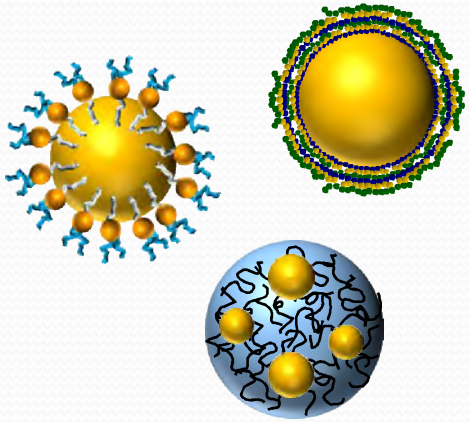
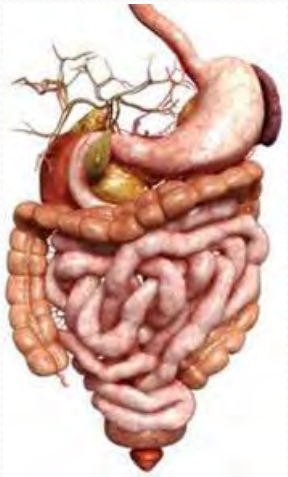
Hilditch Memorial Lecture:

Improving Food Emulsion Functionality through Structural Design Principles

UMASS AMHERST





David Julian McClements

Department of Food Science

University of Massachusetts

Food Design: The Traditional Method

~ 4000 BCE

~ 2300 BCE

~ 200 BCE

Many familiar foods are the result of hundreds or thousands of years of development and were largely created by chance, art and craft

Food Design: The “Star Trek” Method

Starship Enterprise

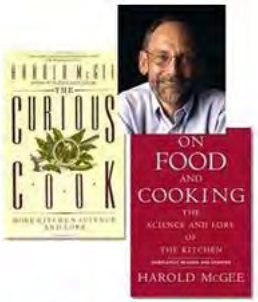
Food Replicator

Food !

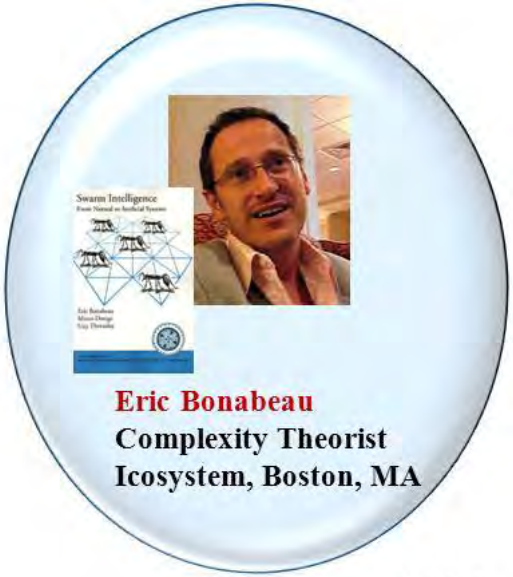
Food Design:

Making “Star Trek” a Reality

Homaru Canto
Chef & TV personality
(Moto Restaurant)

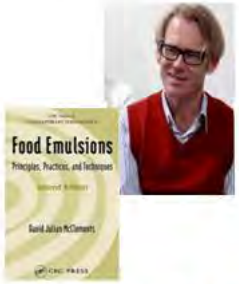


Harold McGee
Food Expert
(Journalist and Author)



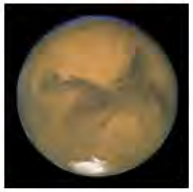
Eric Bonabeau
Complexity Theorist
Icosystem, Boston, MA

Leroy Chiao
(International Space Station Commander)



David Julian McClements
Emulsion Scientist
(Food Science Professor)

NASA



Mars

Icosystem, Boston, MA

3-D Printer: Printing Foods

The "Star Trek" Method

Layer-by-layer printing of foods

http://www.evilmadscientist.com/article.php/3printerpreview

https://sites.google.com/a/cornell.edu/fahteam/home

http://www.designboom.com/weblog/cat/16/view/11012/amit-zoran-cornucopia-food-printer.html

Models for Food Design: Emulsions

Input Parameters

Formation

Homogenization

ÅDesign, Pressure, Passes

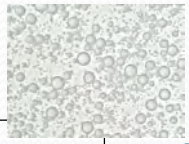
Phase Properties

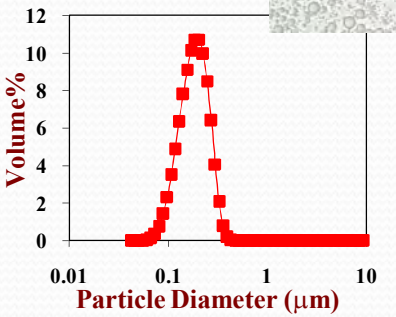
Åη, ρ, γ, ***n***, ε

Surfactant Properties

ÅC, Γ, π, kinetics, charge

Output Parameters





Stability & Properties

Droplet Characteristics

ÅConcentration

ÅSize distribution

ÅInterfacial properties

Åthickness, charge, polarity

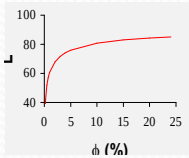
ÅInteractions

ÅSpatial organization

Output Parameters

Appearance

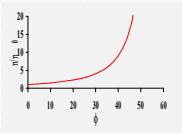
ÅL,a,b



Texture

Å***G*, *Y*, Y_f**

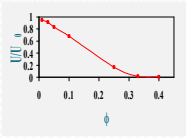
Åη ***vs.*** τ



Shelf Life

Å***d* = *f*(*t*)**

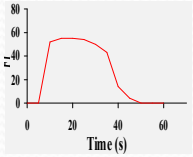
Åϕ = ***f*(*t*,*h*)**



Flavor

ÅHeadspace

Å***FI* vs. *t***



ÅEmpirical Knowledge

ÅAnalytical Theory

ÅComputer Simulations

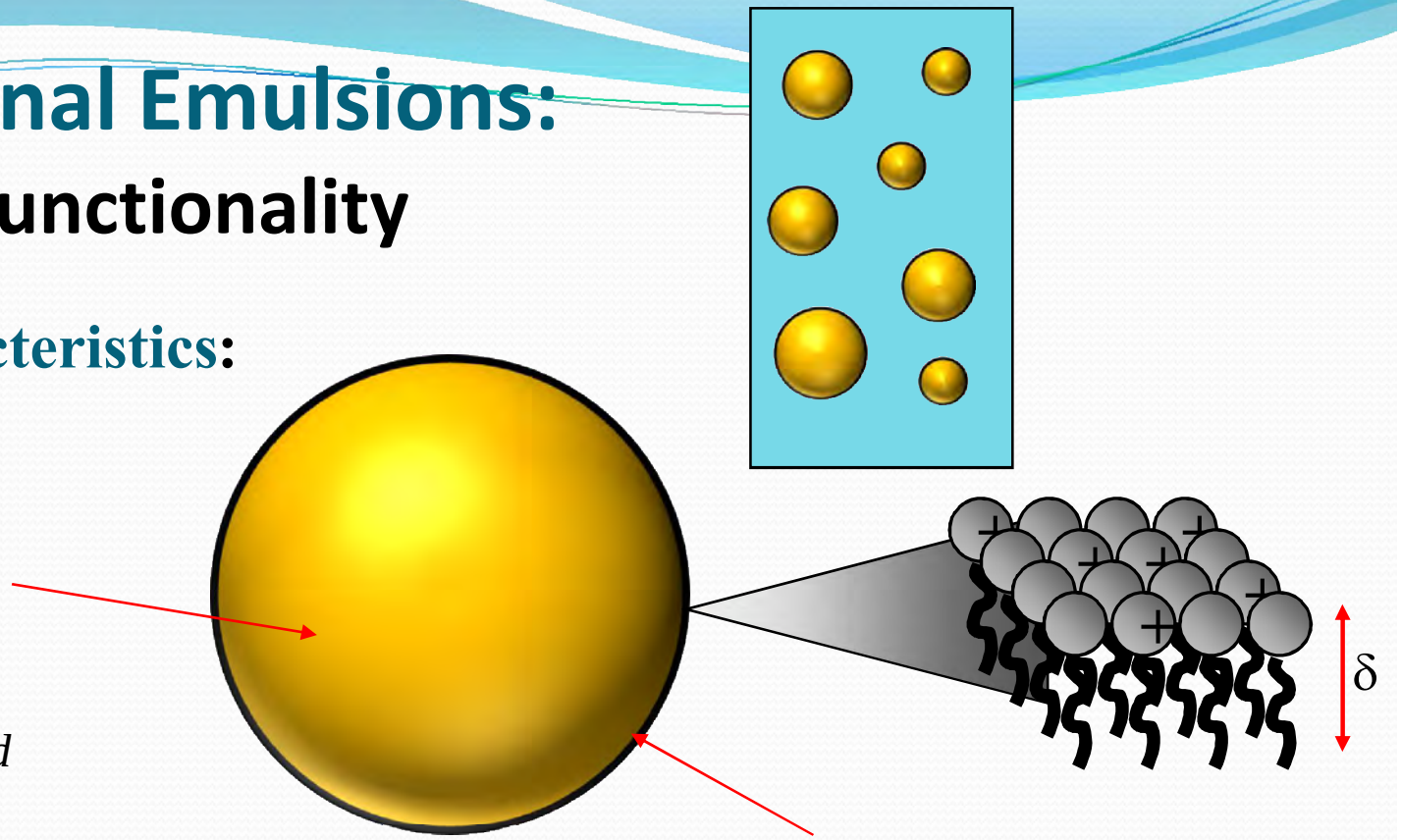
ÅStatistical Correlations

Conventional Emulsions:

Designing Functionality

Particle Characteristics:

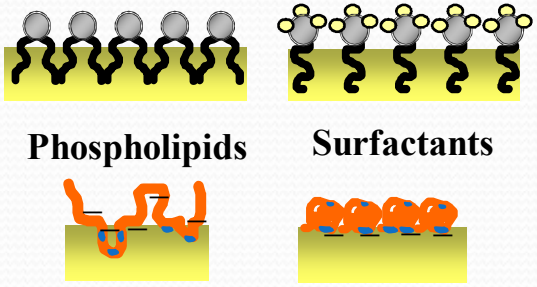
- **Lipid Composition**
  - *Polarity*
  - *Density*
  - *Viscosity*
- **Size Distribution**
- **Physical state**
  - *Solid vs. Liquid*



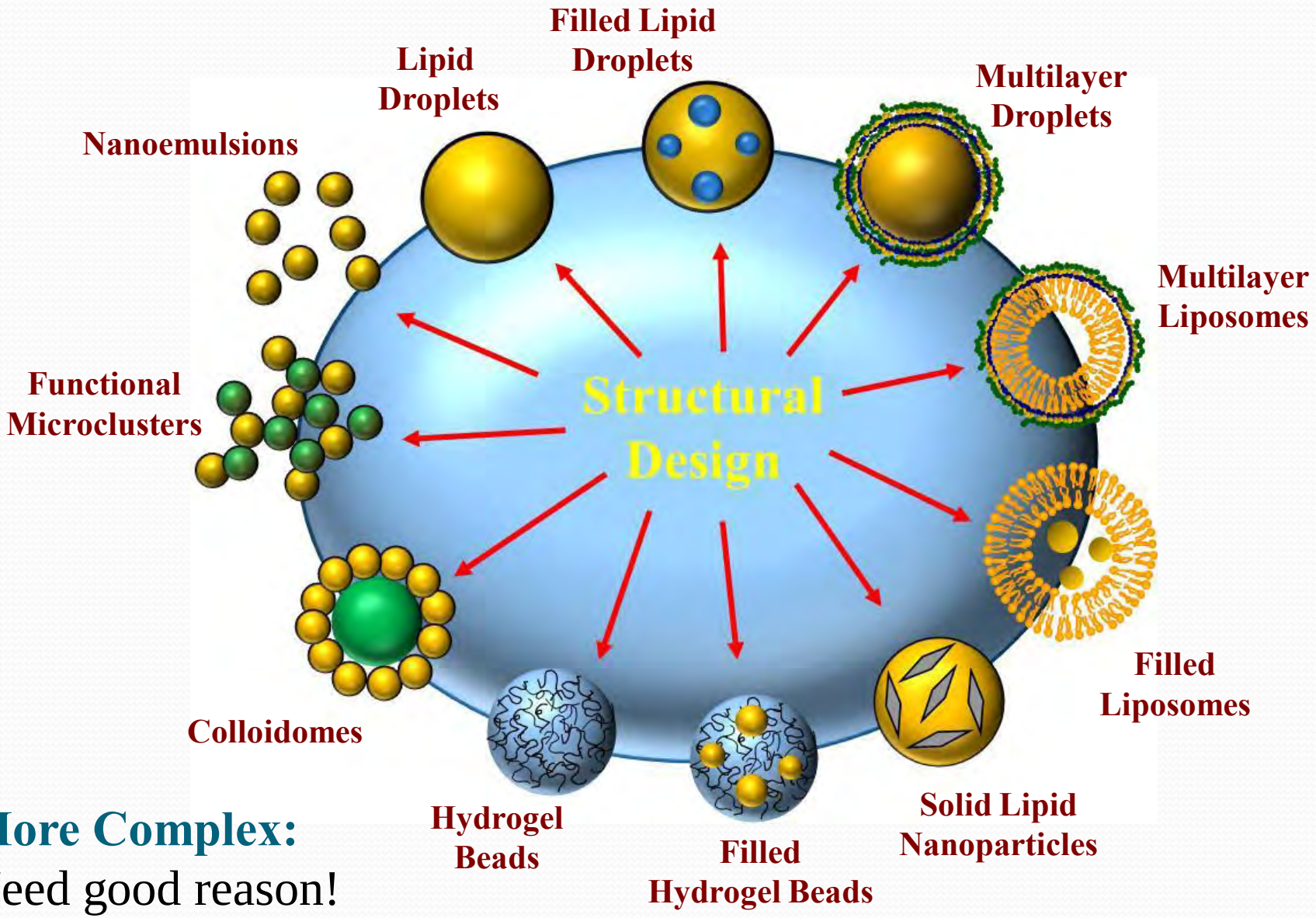
Interfacial Characteristics:

- **Charge**
- **Thickness**
- **Chemistry**
- **Responsiveness**

Limited Number of Food-Grade Emulsifiers



Structured Emulsions: Designing Functionality



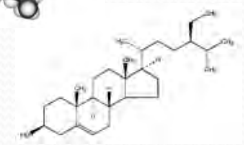
More Complex:

Need good reason!

Encapsulation of Bioactives:

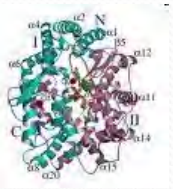
Ingredients & Challenges

Lipids



- Flavors (*e.g.*, citral, limonene)
- Unsaturated Fats (*e.g.*, ω-3, CLA)
- Phytosterols & Phytostanols (*e.g.*, Sitostanol)
- Carotenoids (*e.g.*, lycopene, β-carotene, zeaxanthin)
- Vitamins (*e.g.*, A and D)

Biopolymers



- Dietary fibers (*e.g.*, chitosan, gums)
- Peptides (*e.g.*, ACE inhibitors, satiety)
- Proteins (*e.g.*, immunoglobulins)

Microorganisms

- Probiotics

Minerals

- Calcium, Iron Fe^{2+}

Potential Challenges:

- Low water solubility
- Crystalline
- Chemical instability
- Enzyme digestibility
- Low bioavailability
- Flavor modulation
- Matrix compatibility

Need to Understand Specific Ingredient Characteristics and Identify Specific Challenges

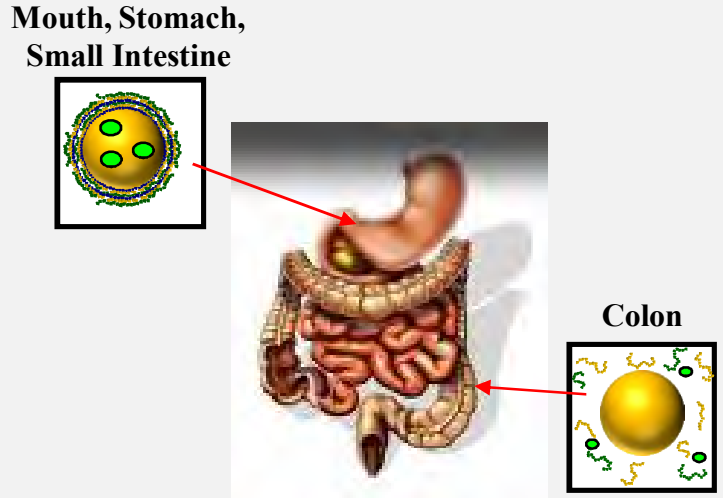
Controlled Bioavailability:

Designing Emulsions to Control Biological Fate of Bioactive Agents

Controlled & Targeted Release

- **Tunable stability/instability profiles**
  - *Encapsulation and release of functional components in response to specific environmental triggers (pH, enzymes, I)*

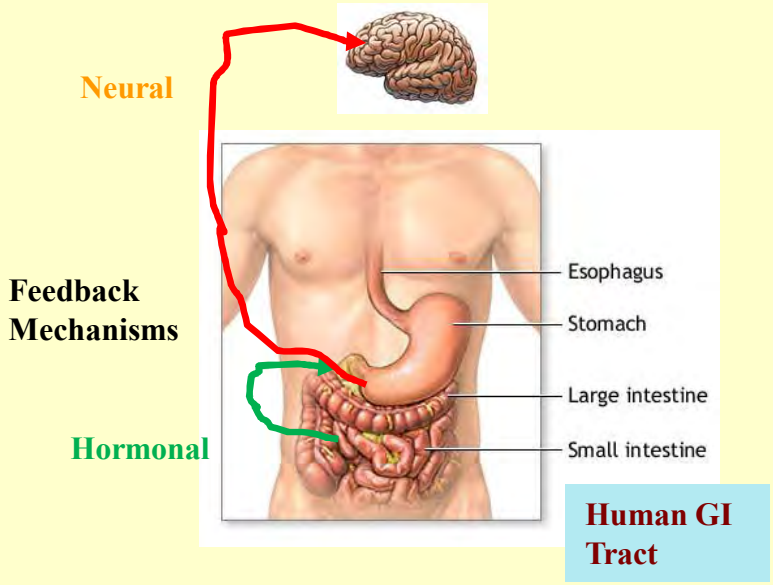
- Deliver bioactive components to site of action: mouth, stomach, small intestine or colon



Modulating Satiety

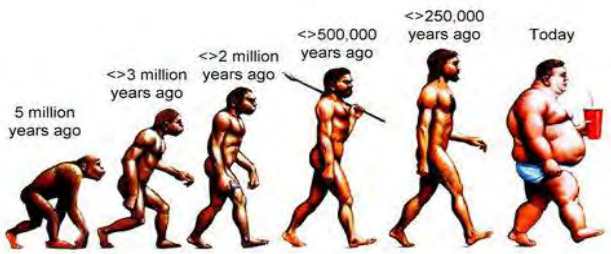
- **Acid stable foods**
  - *Even distribution of fat in stomach*
- **Delay digestion**
  - *-Deliver more undigested nutrients to ileum*

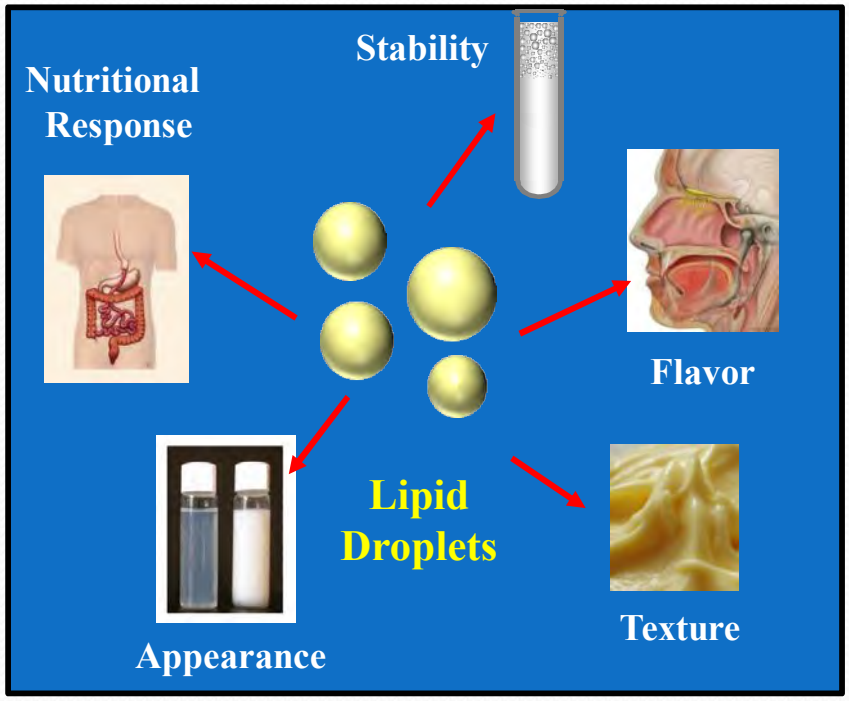
- Generate neural & hormonal signals that enhance satiety, thereby reduce amount of food consumed



Reduced Calorie Products:

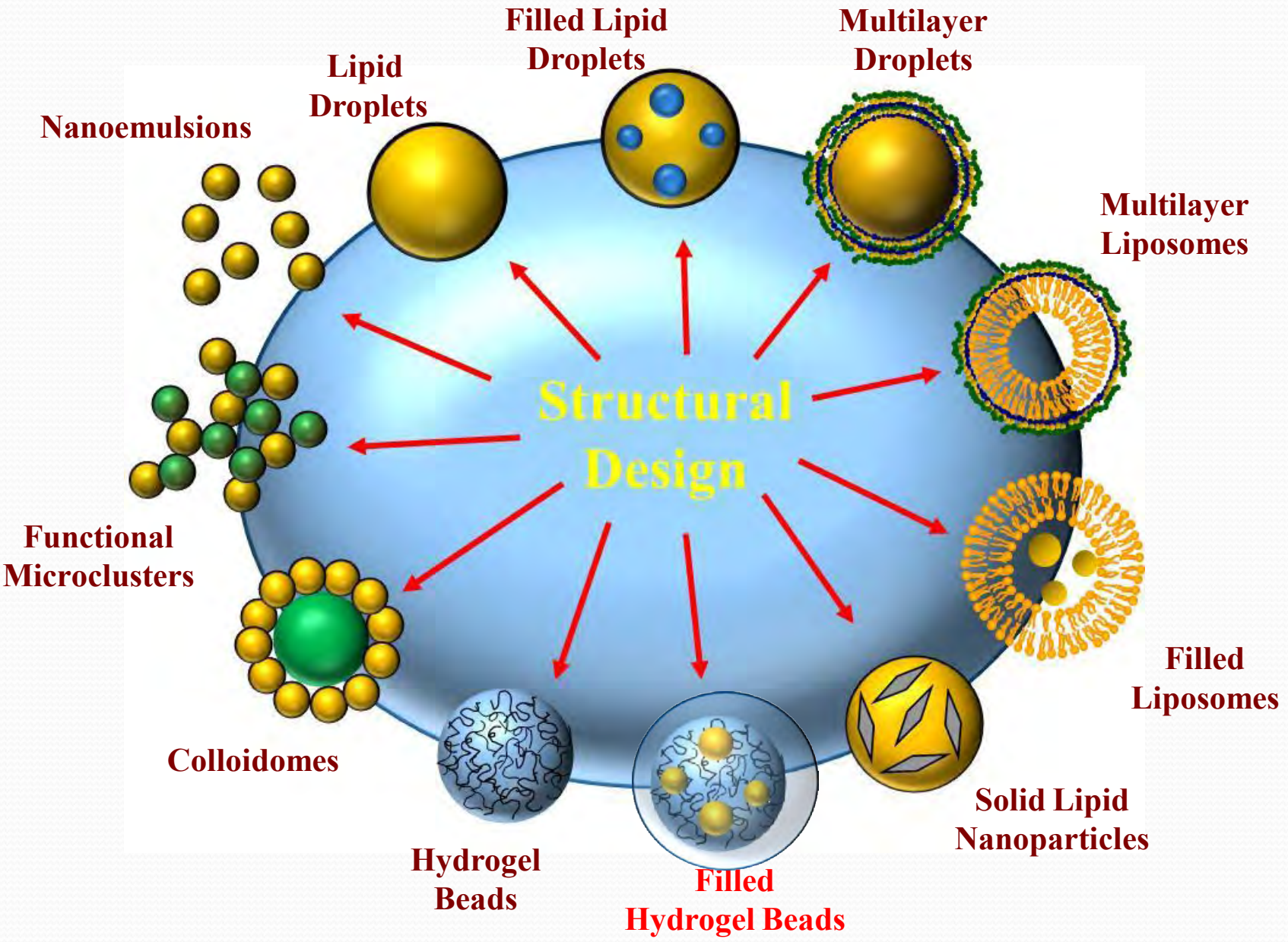
Designing Emulsions to Improve Quality and Health





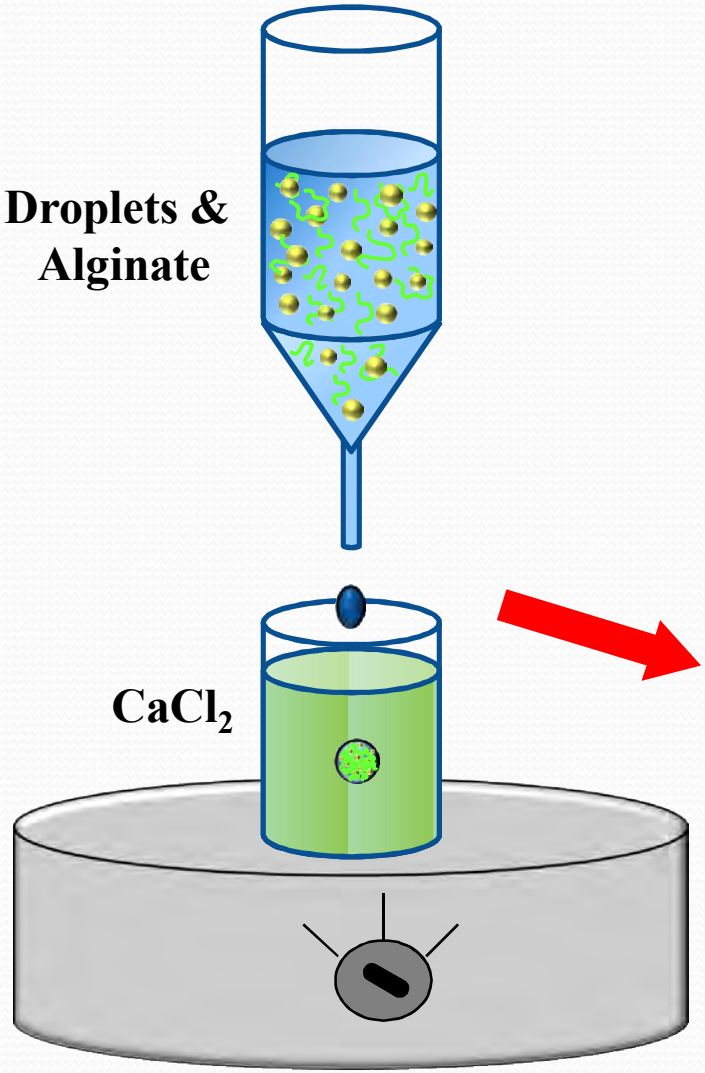
Lipid droplets play multiple roles in determining the physicochemical & physiological properties of emulsion-based food products.

Structured Emulsions: Filled Hydrogel Particles



Filled Biopolymer Particles:

Extrusion Methods

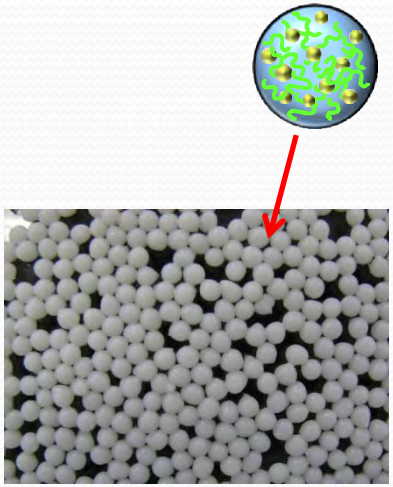


Controllable Properties

ÅDroplet size & loading

ÅBead dimensions

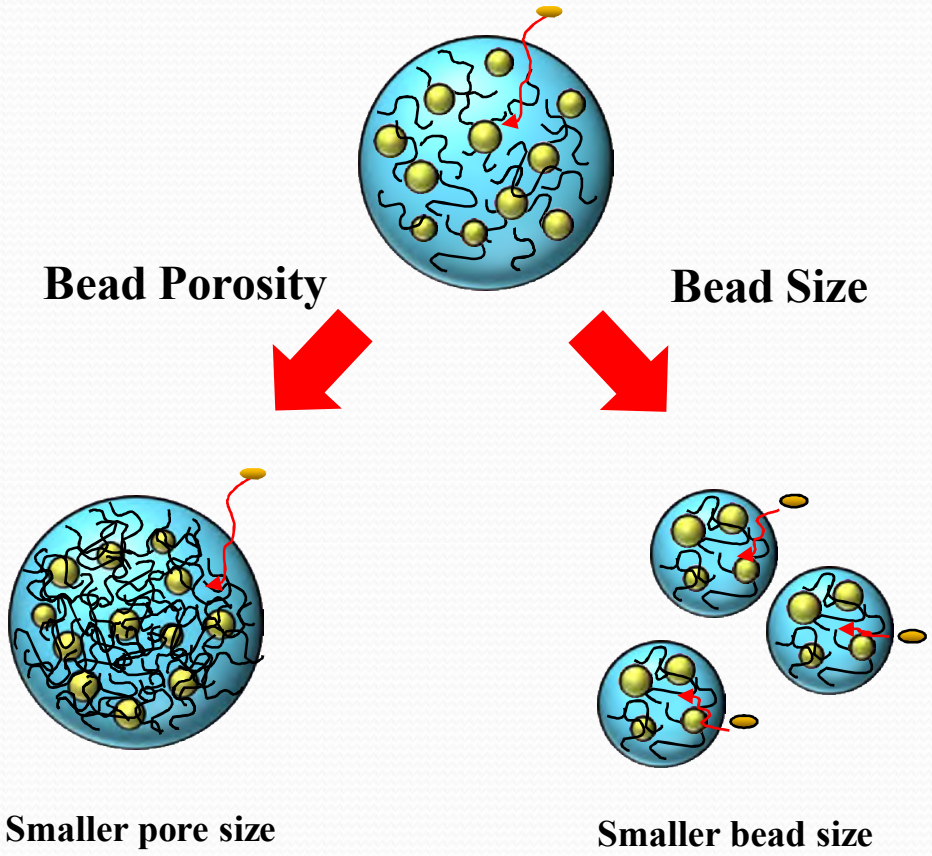
ÅBead pore size



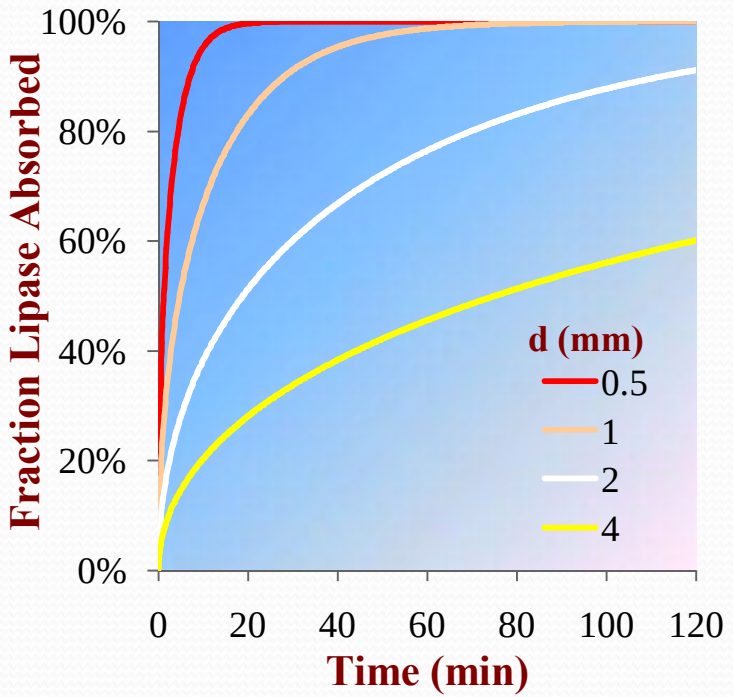
Calcium Alginate Beads

Filled Hydrogel Particle Design:

Methods to Control Digestibility



$$\Phi = \frac{M(t)}{M(\infty)} = 1 - \frac{6}{\pi^2}\sum_{n=1}^{\infty}\frac{1}{n^2}\exp\left(-\frac{D_{gel}n^2\pi^2 t}{a^2}\right)$$

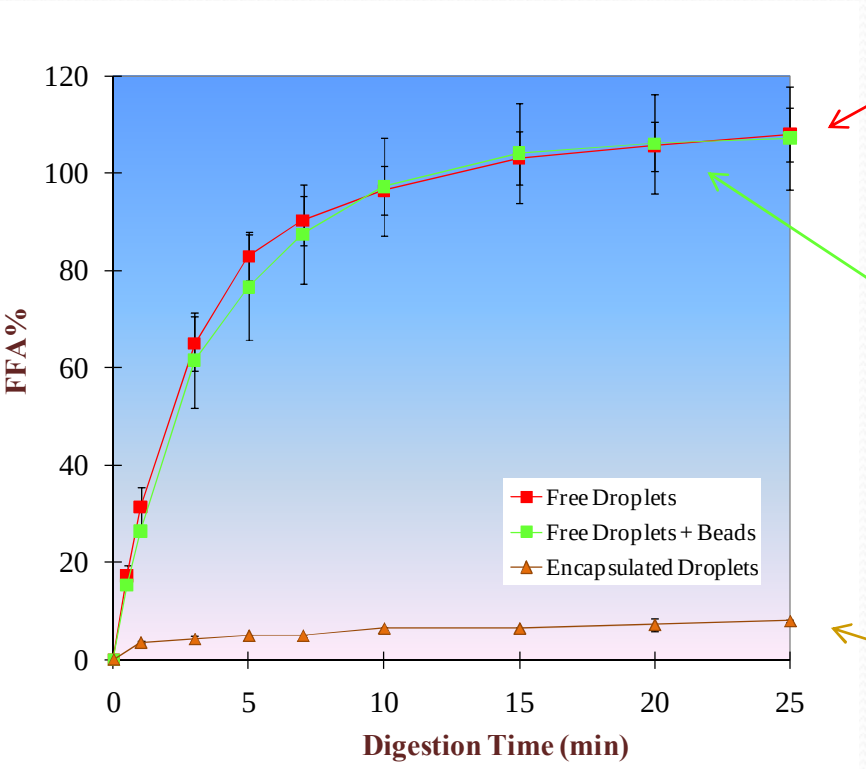


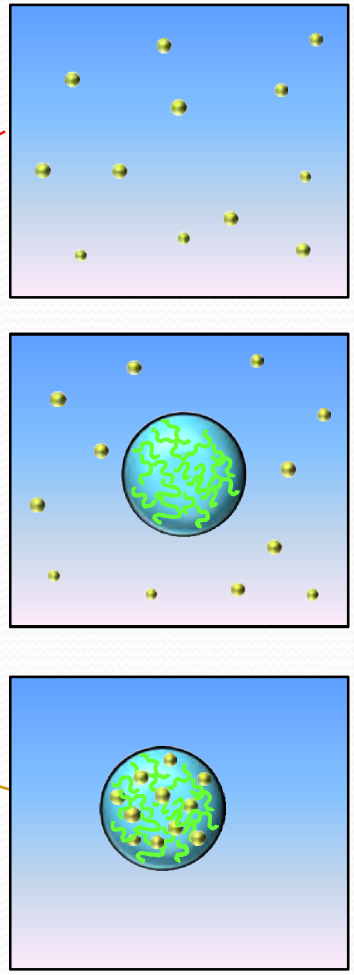
Physicochemical Basis of Bioavailability

Controlling Digestibility

pH-Stat

Å FFA-time profile

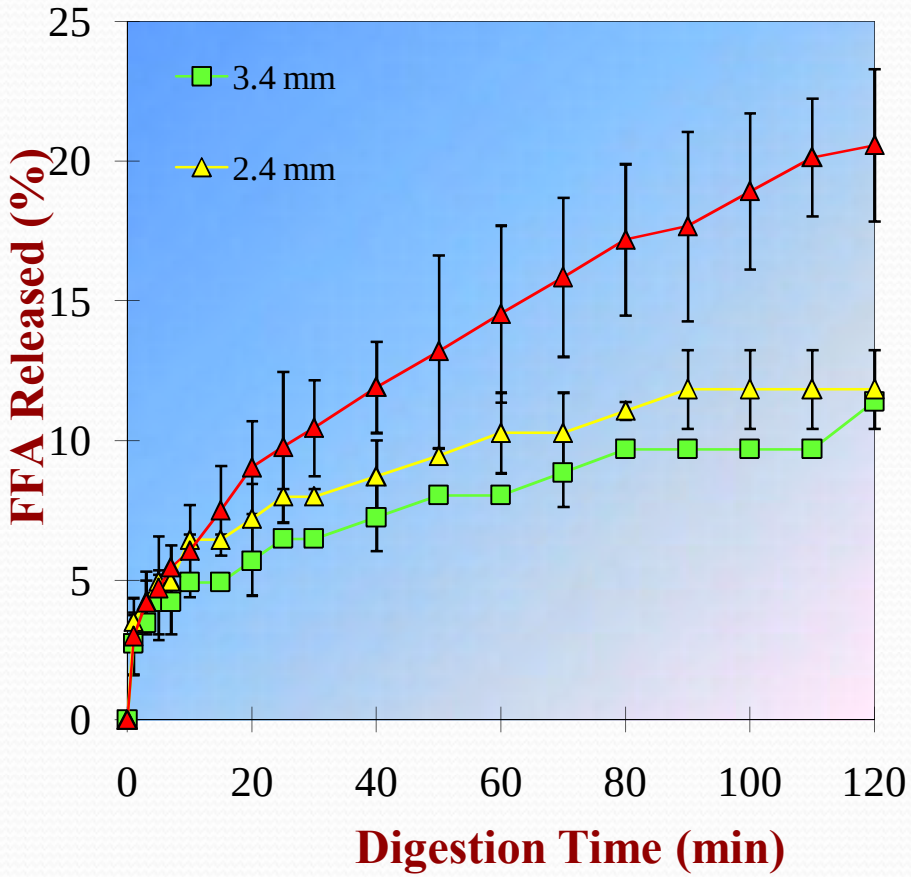


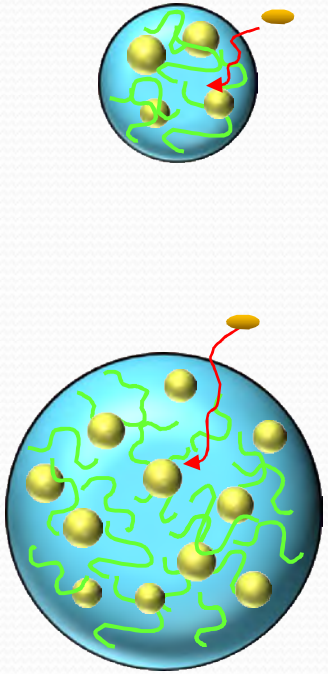


Filled calcium alginate beads can control digestibility

Filled Biopolymer Particles

Effect of Bead Size

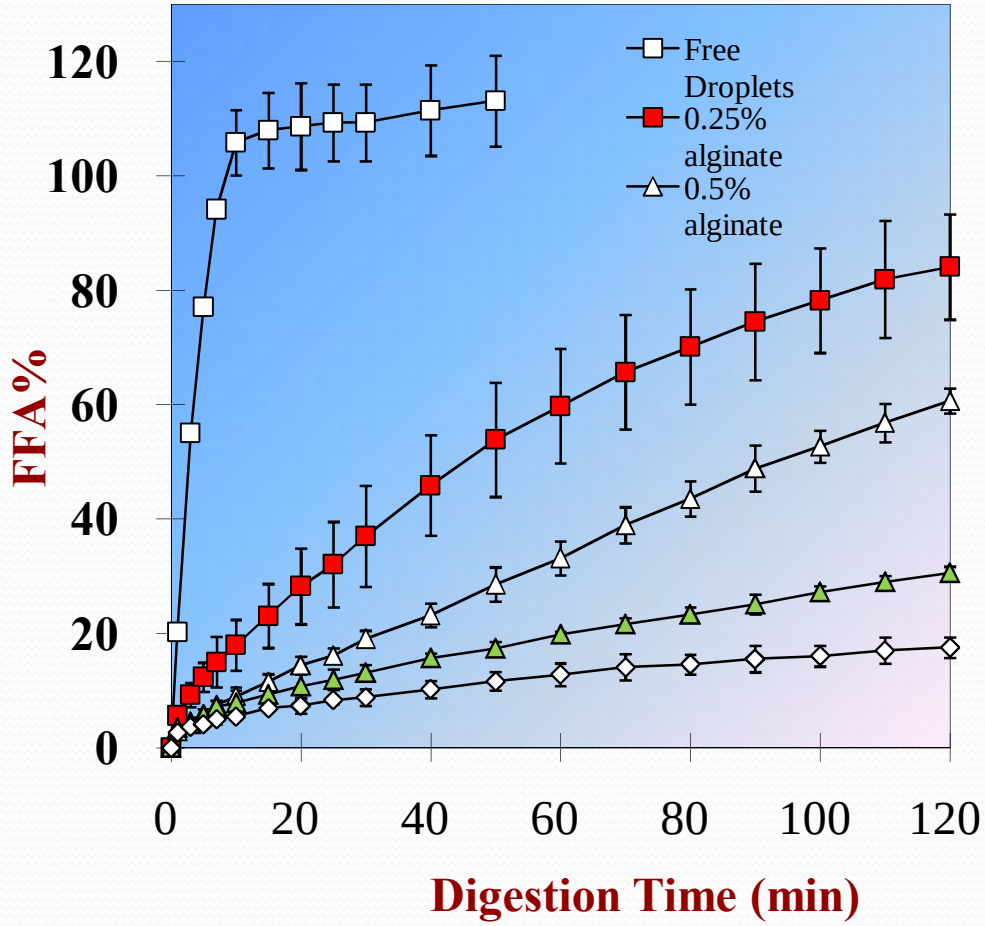


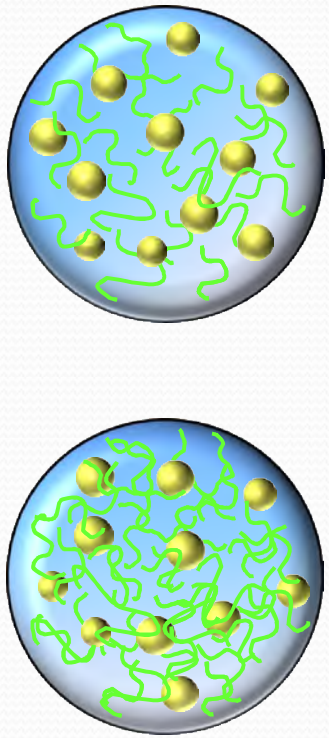


Filled calcium alginate beads

Filled Biopolymer Particles

Effect of Bead Cross-linking

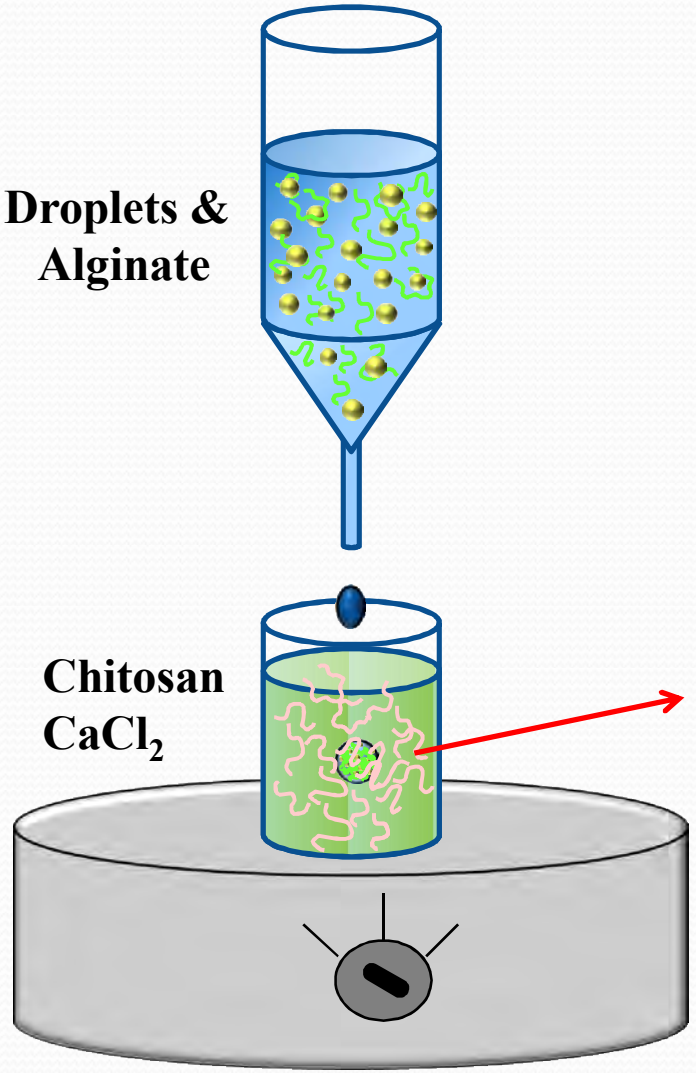




Filled calcium alginate beads

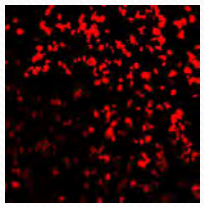
Filled Biopolymer Particles

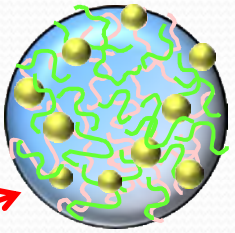
Coacervation Methods



Controllable Properties

- Droplet size & loading
- Bead dimensions
- Bead pore size

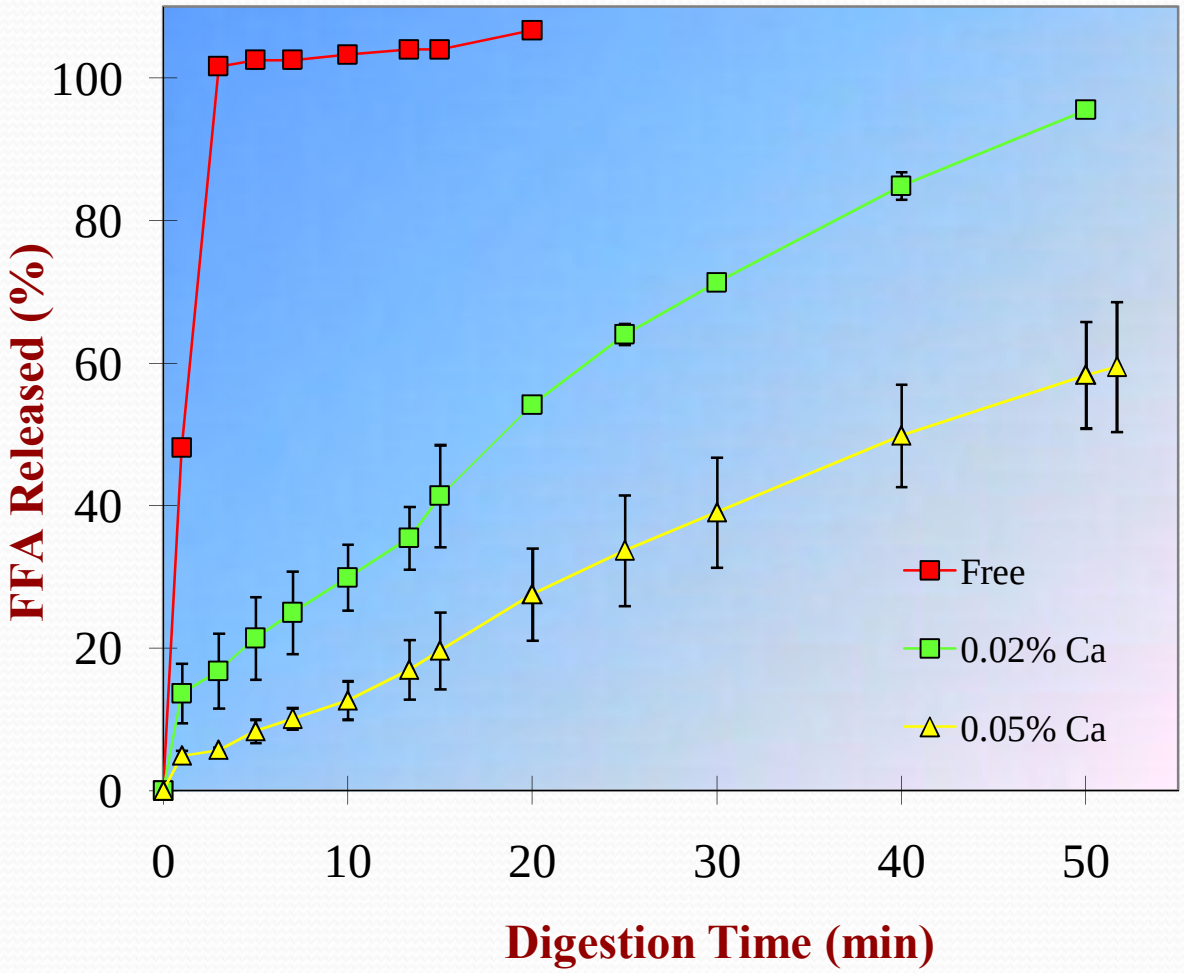


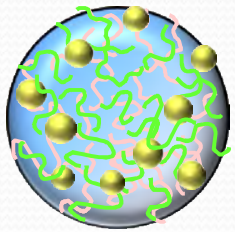


Calcium-Alginate-Chitosan
Coacervates

Coacervates

Effect of Cross-linking

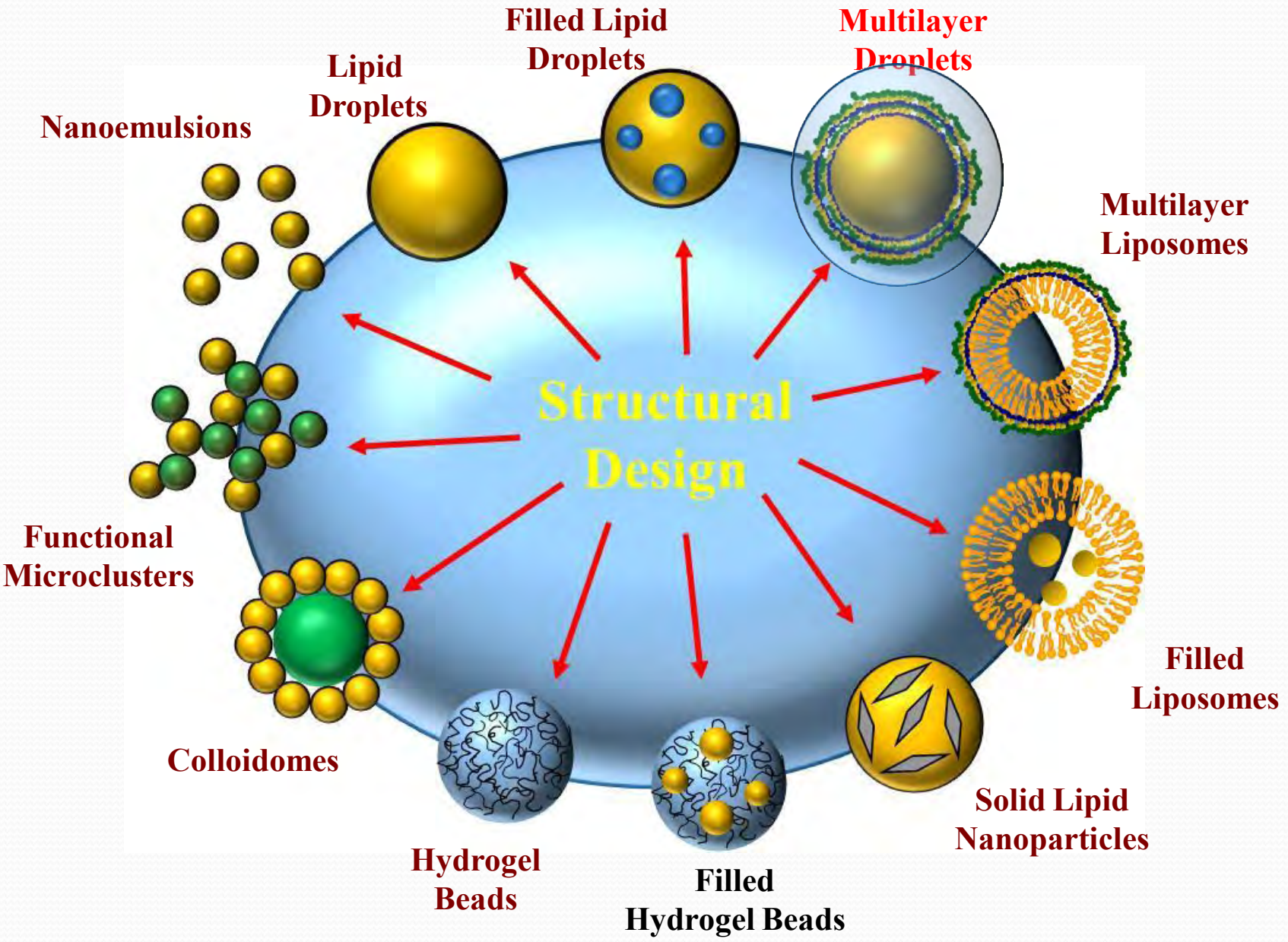




Filled chitosan-alginate coacervates

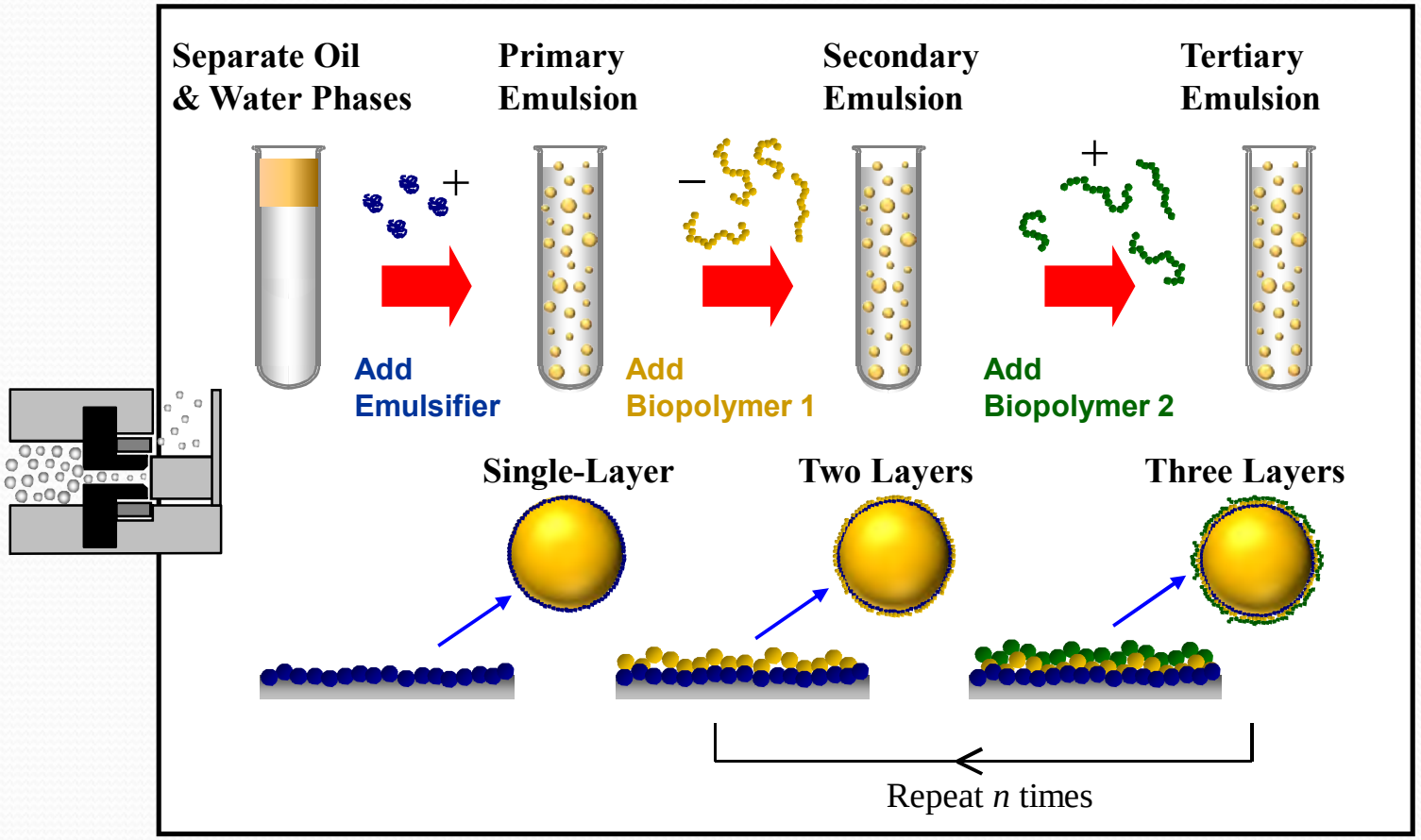
d = 100 μm

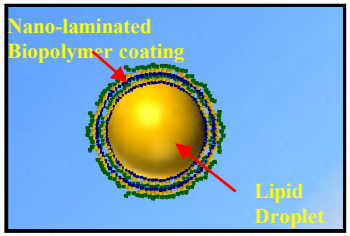
Structured Emulsions: Multilayer emulsions



Multilayer Emulsions:

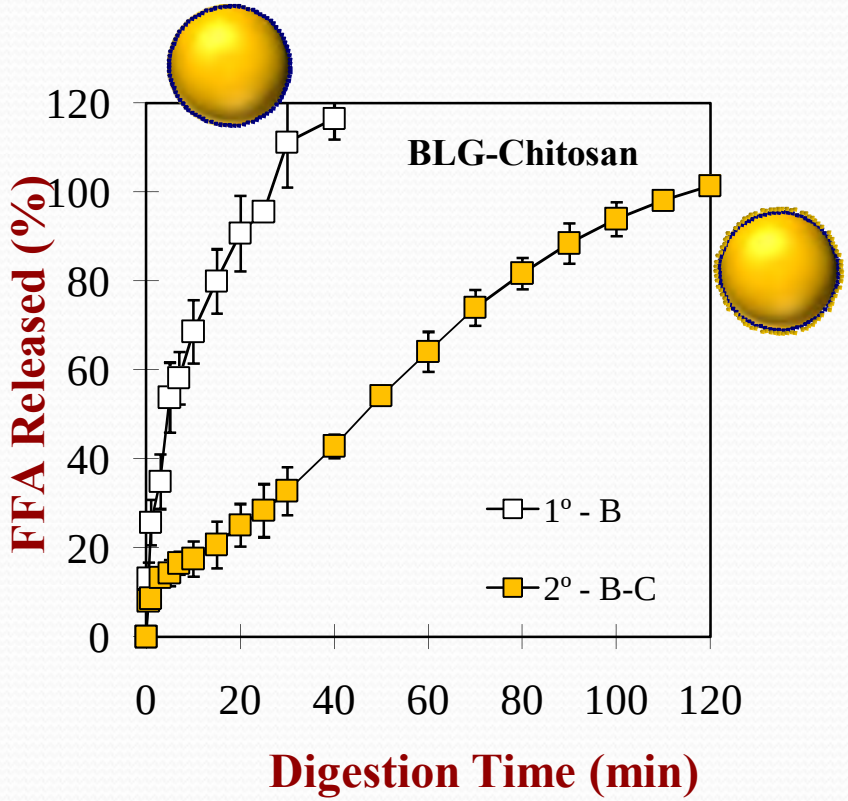
Formation using LbL Method

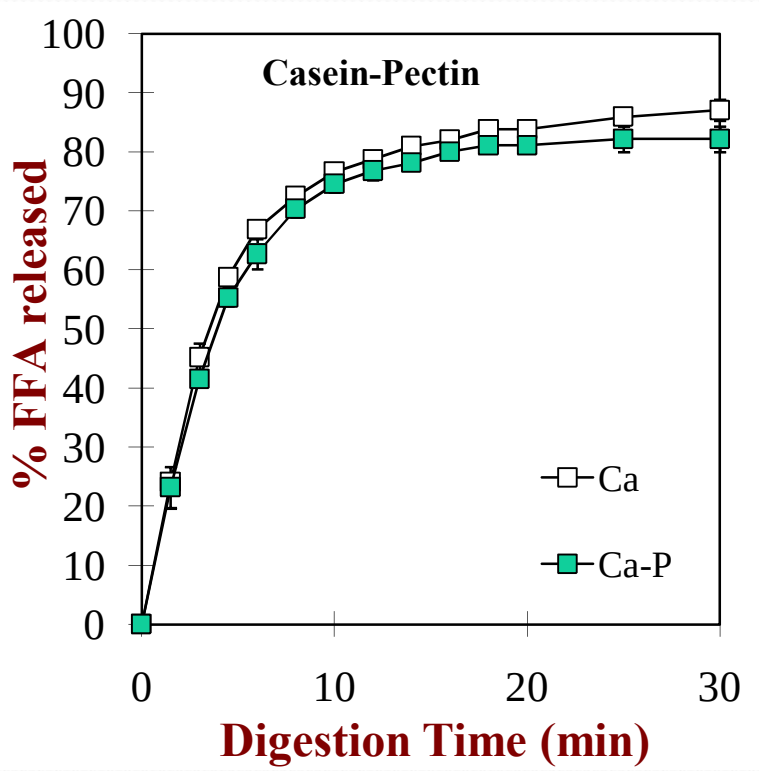




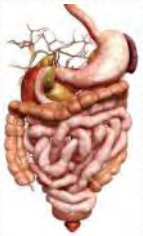
Applications of Multilayer Emulsions

Digestibility in *In Vitro* Model

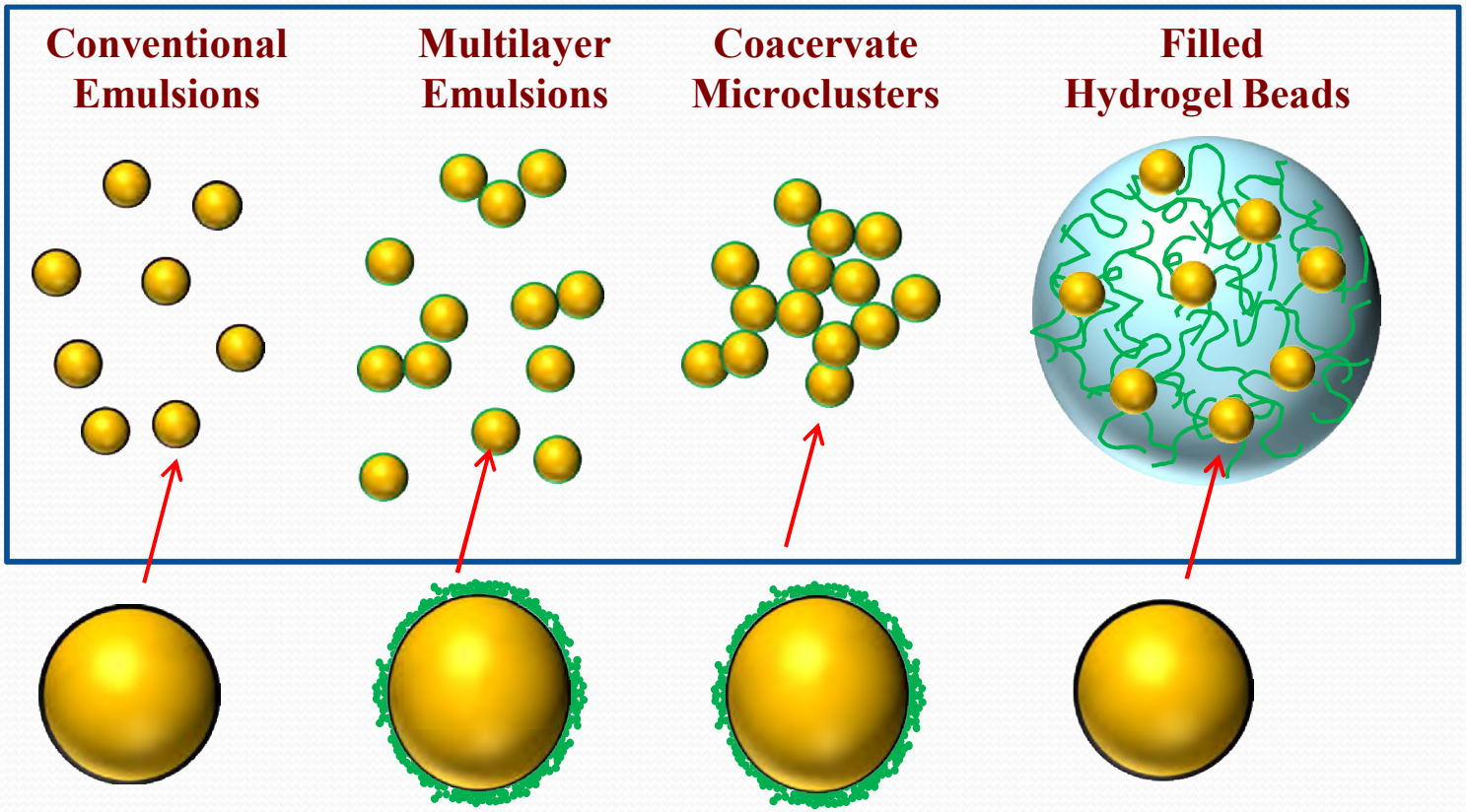




Digestion depends on multilayer properties



Comparison of Structuring Approaches for Controlling Digestion: In vivo - In vitro Comparison



(A) conventional emulsion; (B) multilayer emulsion; (C) coacervate microclusters; (D) filled hydrogel beads fabricated from corn oil, whey protein, chitosan and/or alginate.

Comparison of Hydrogel Particles

In vivo *versus* In vitro comparisons

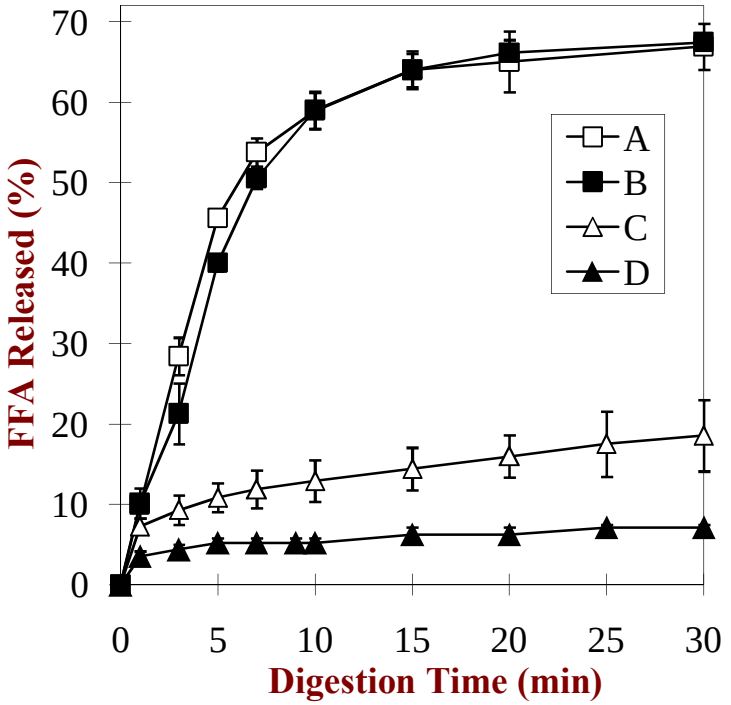
Conventional	A	S	SI1	SI2	SI3
Multilayer	B				
Coacervate microcluster	C				
Filled hydrogel	D				

Initial **Stomach** **Small Intestine**

Comparison of Hydrogel Particles

In vivo *versus* In vitro comparison

In vitro ï pH stat

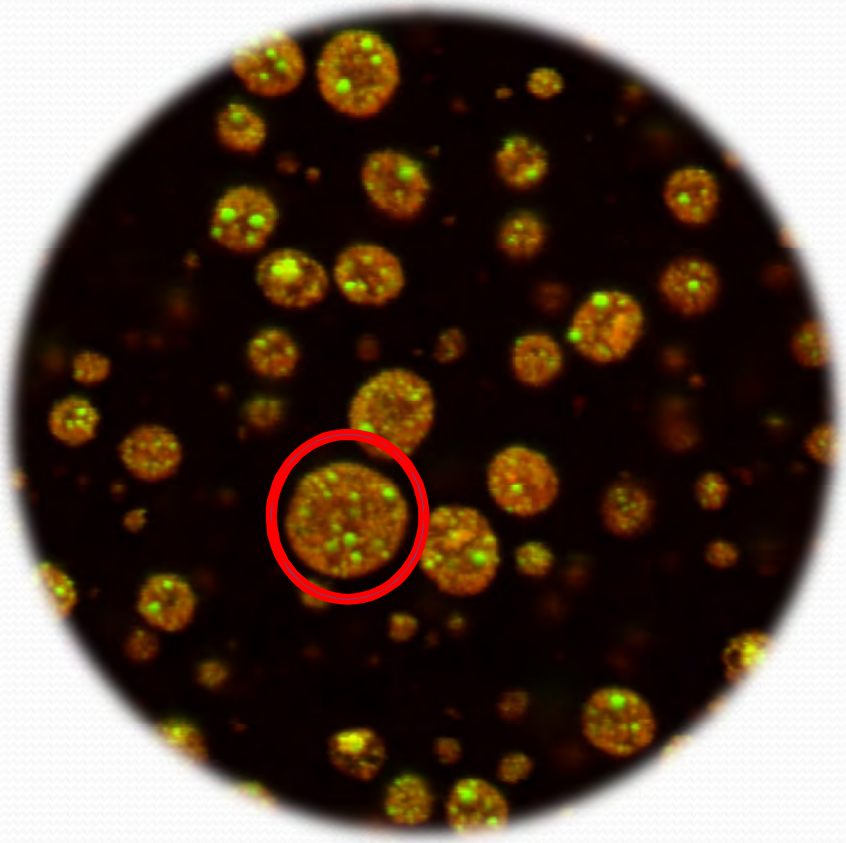


In vivo – fatty acid marker in body

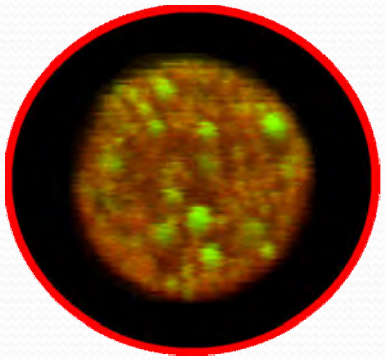
Sample	Serum	Jejunum
A - Conventional	59 ± 12	28 ± 6
B ï Multilayer emulsion	12 ± 3	14 ± 3
C ï Coacervate microcluster	5.5 ± 2.4	7.0 ± 1.8
D ï Filled hydrogel	0.9 ± 0.6	1.9 ± 0.8

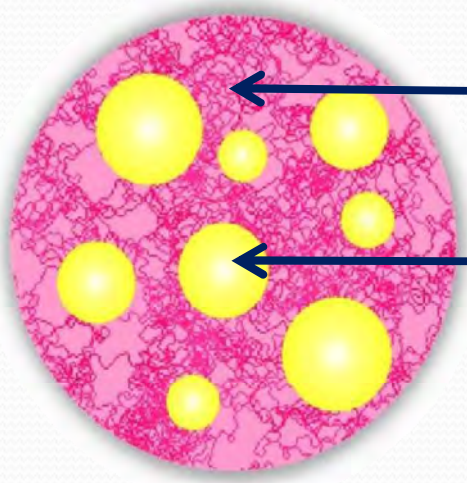
Relative concentration (%) of tridecanoic acid compared to arachidonic acid in serum and jejunum

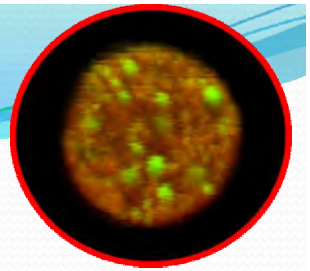
Filled Biopolymer Particles:
Phase Separation-Coacervation Methods



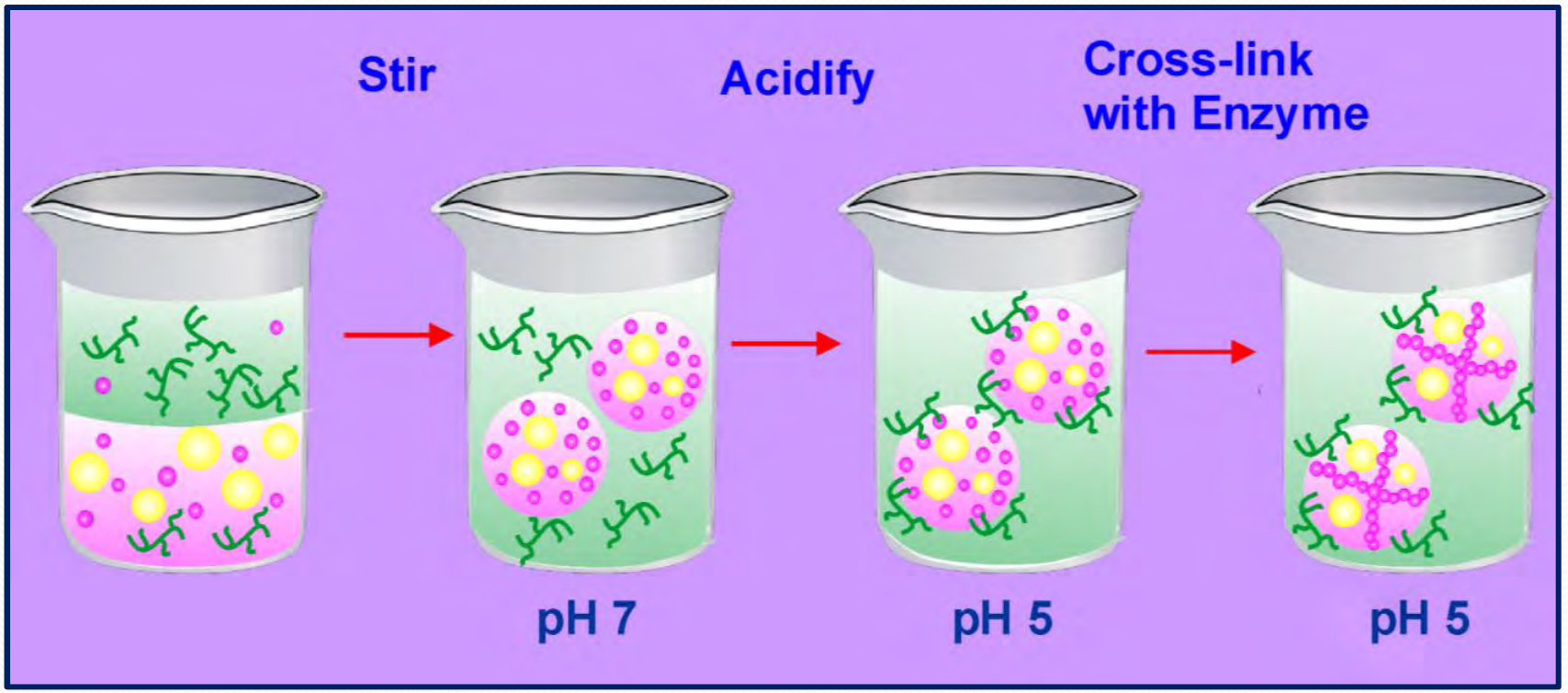
Oil droplets + Casein + Pectin Matrix





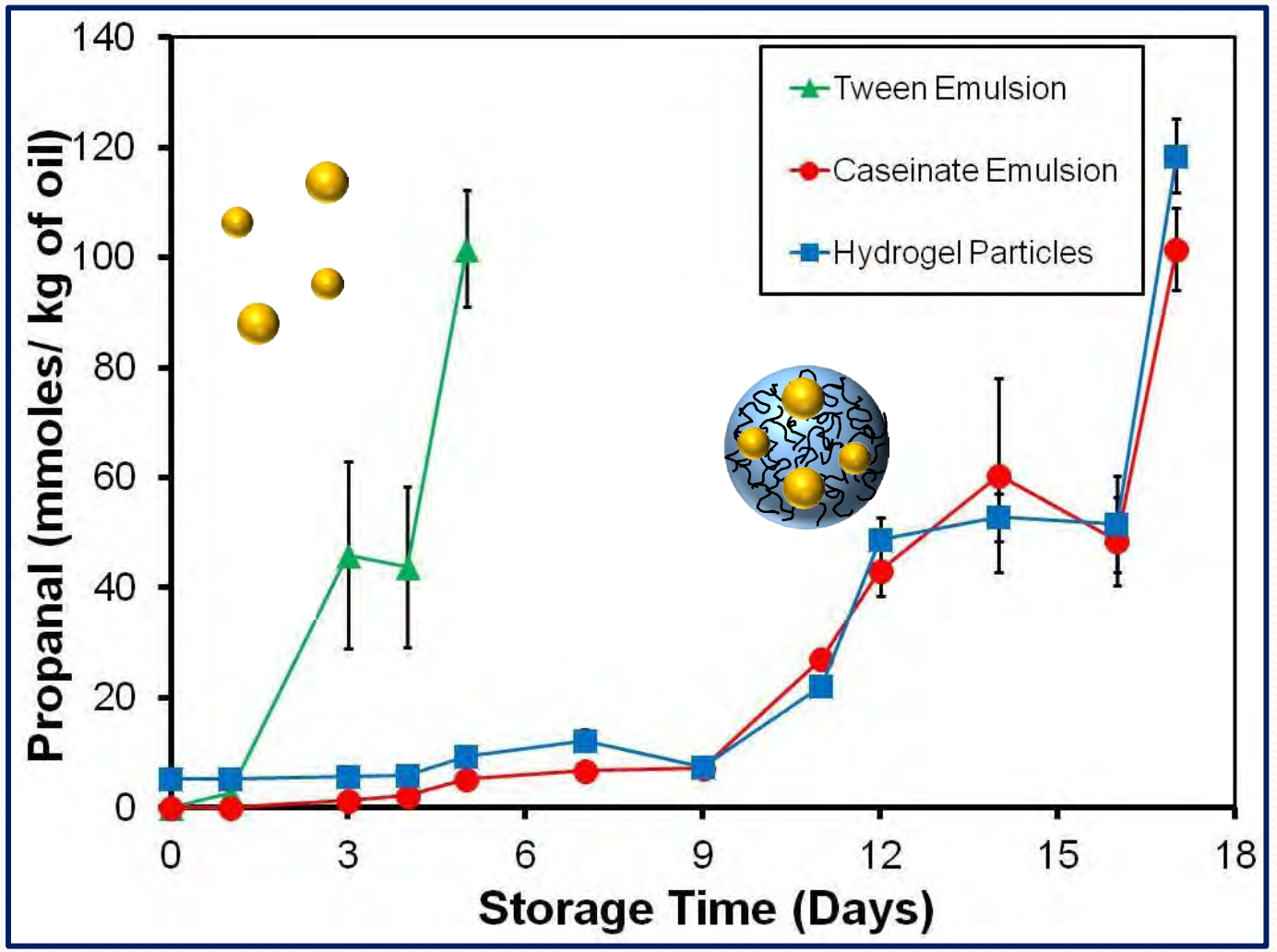


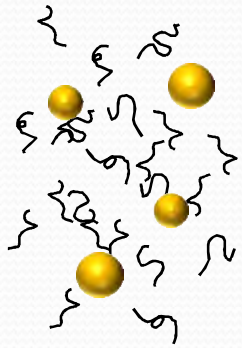
Filled Biopolymer Particles:
Phase Separation-Coacervation Methods



Filled Biopolymer Particles:

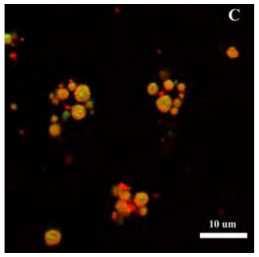
Oxidative stability



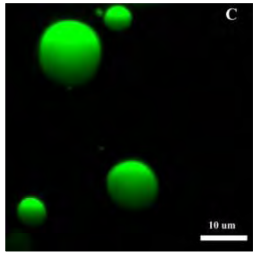


Filled Biopolymer Particles:
In vitro Digestion

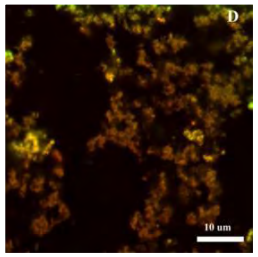
Initial

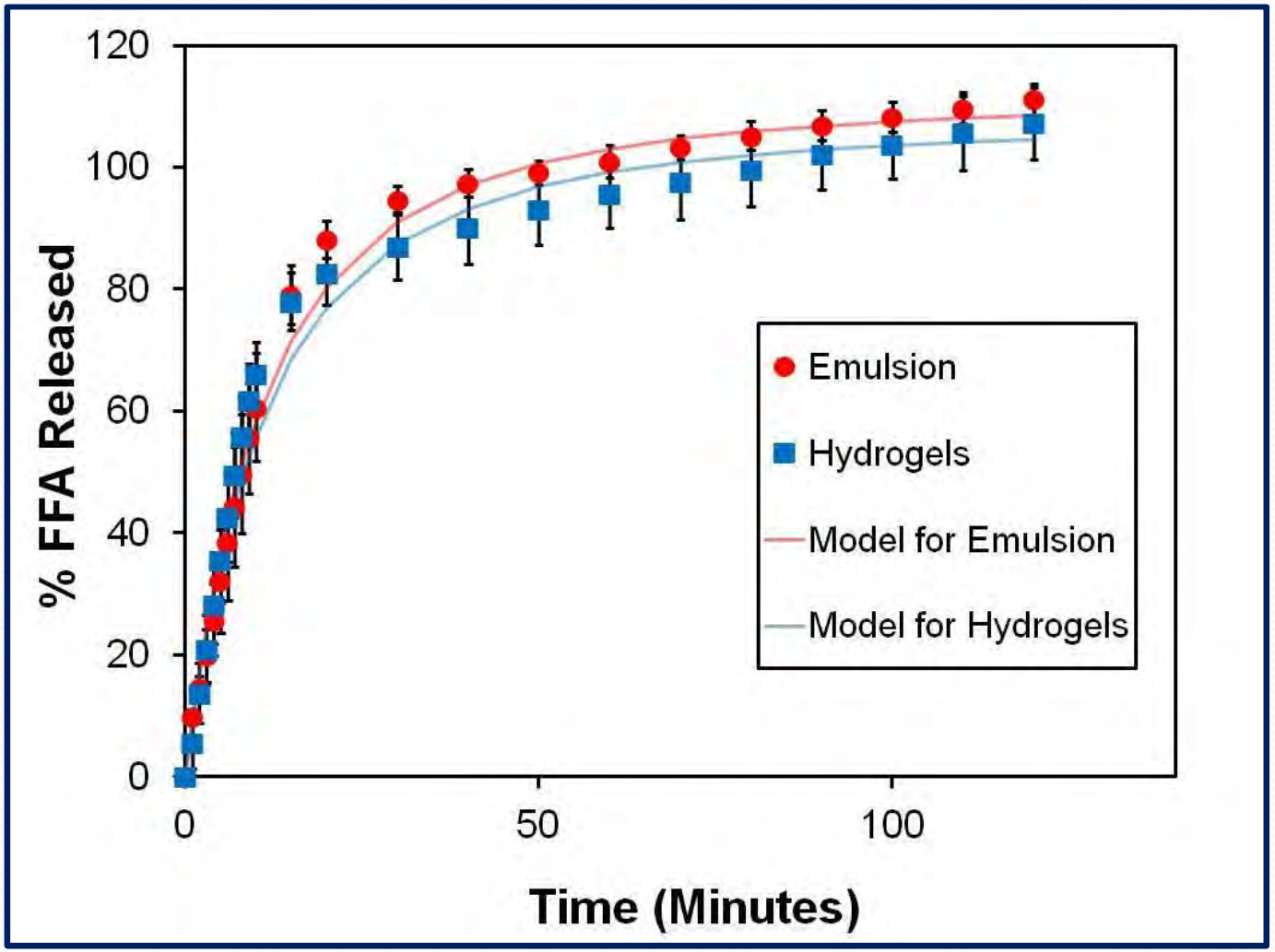


Stomach

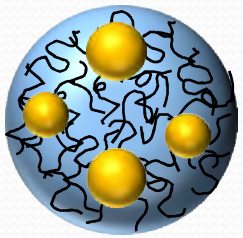


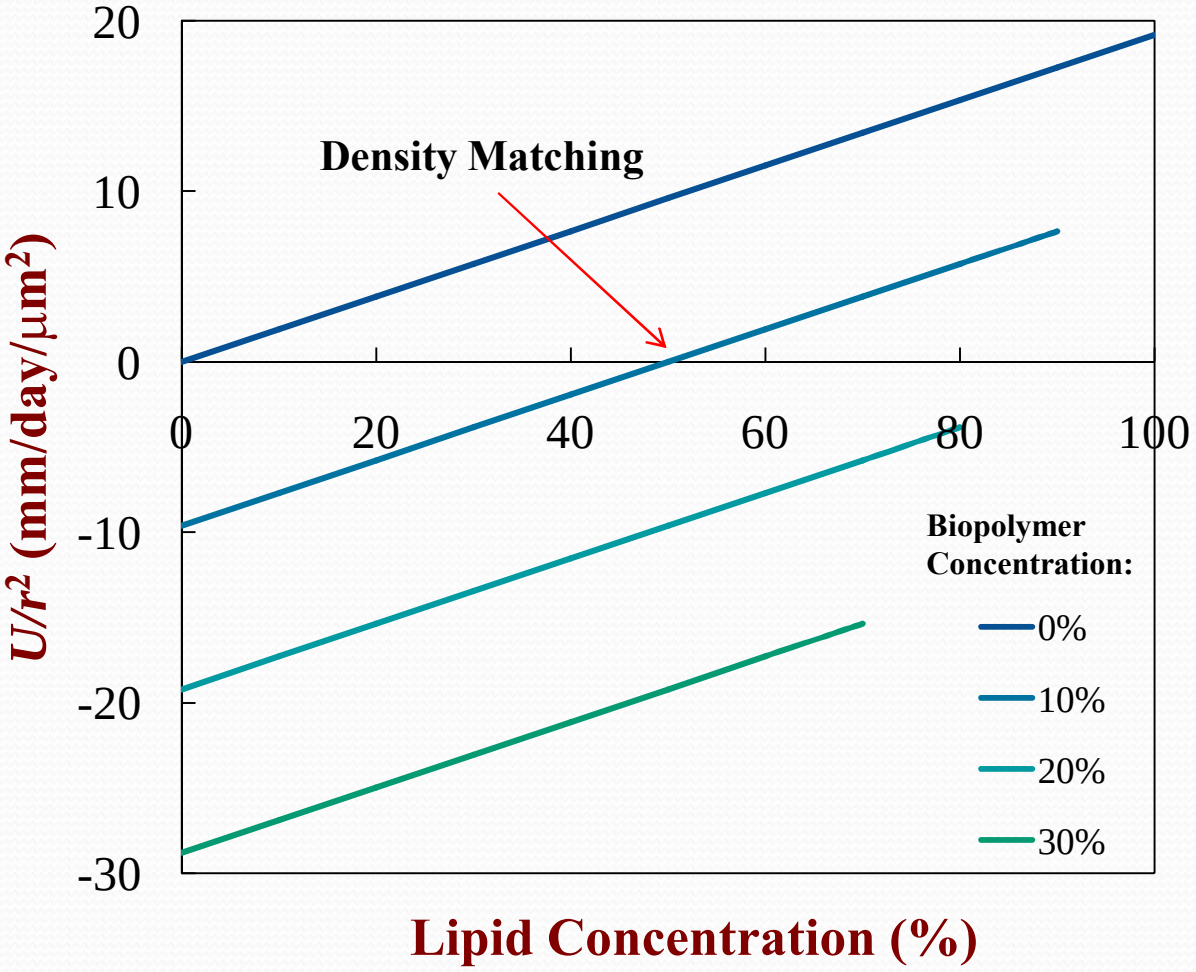
Intestine





Fabricating Density Matched Filled Hydrogel Particles



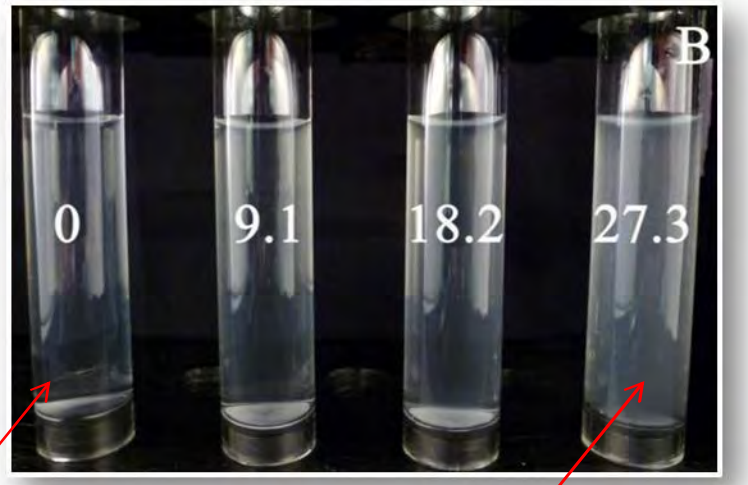


Theoretical prediction of the influence of biopolymer particle composition (lipid and biopolymer concentration) on the stability to gravitational separation. Assumed densities: biopolymer = 1500 kg m^{-3}; water = 1000 kg m^{-3}; oil = 900 kg m^{-3}.

Fabricating Density Matched Filled Hydrogel Particles

Filled Hydrogel Particles with Increasing Oil Levels Prior to Storage (A)

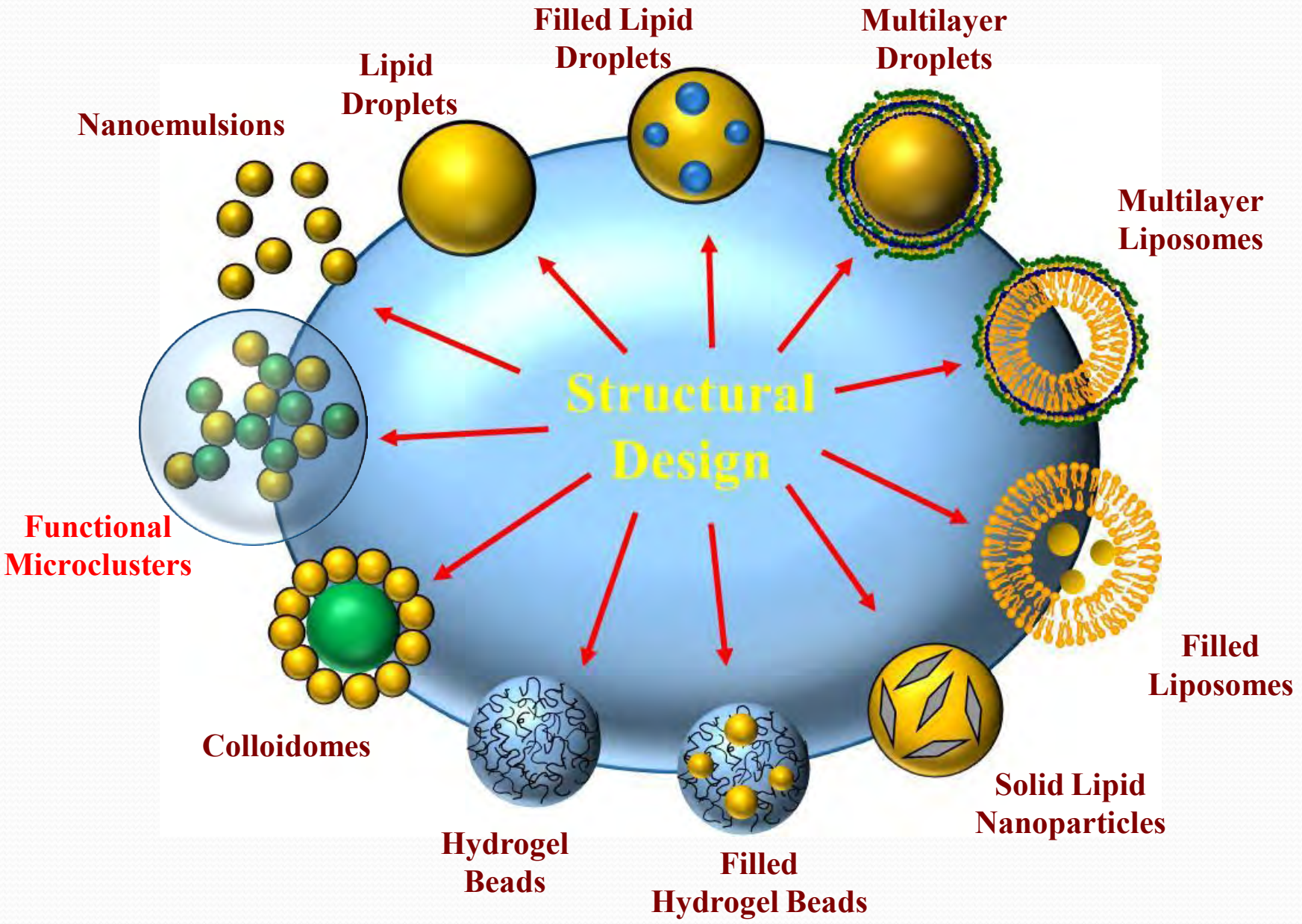
Filled Hydrogel Particles with Increasing Oil Levels After 7 Days of Storage (B)



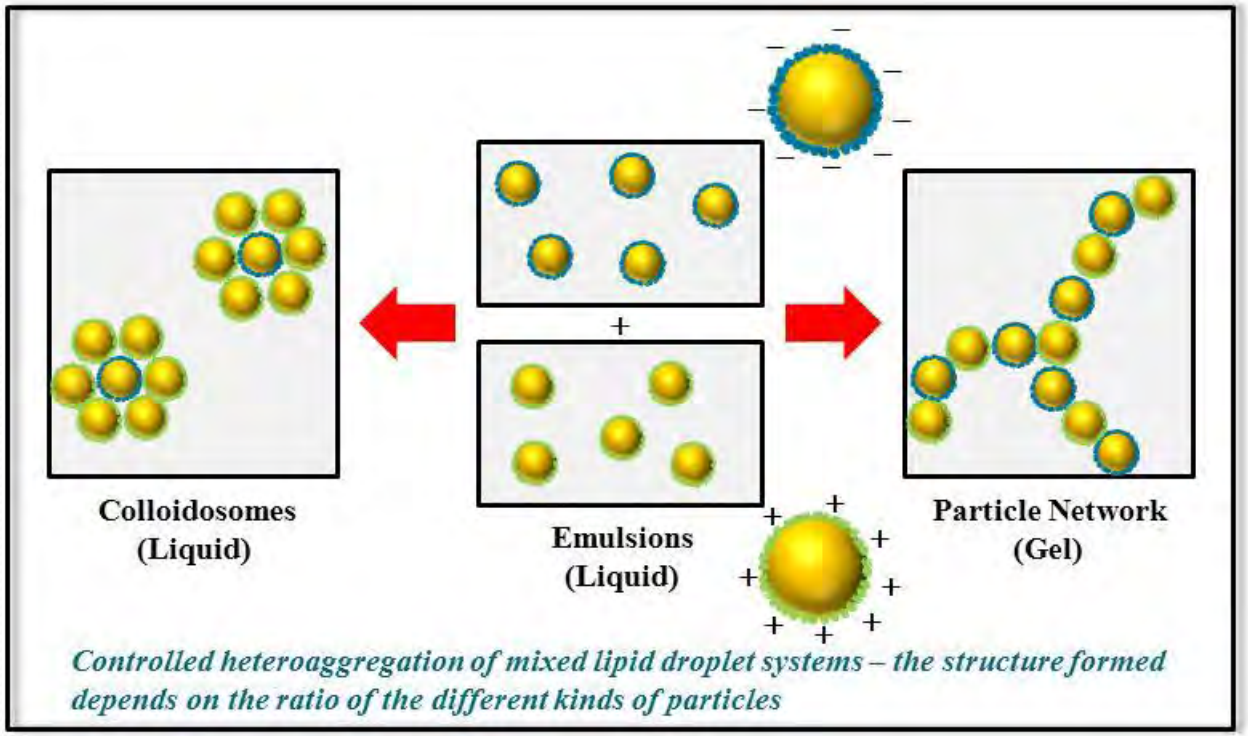
Unstable to sedimentation

Stable to sedimentation (Density matching)

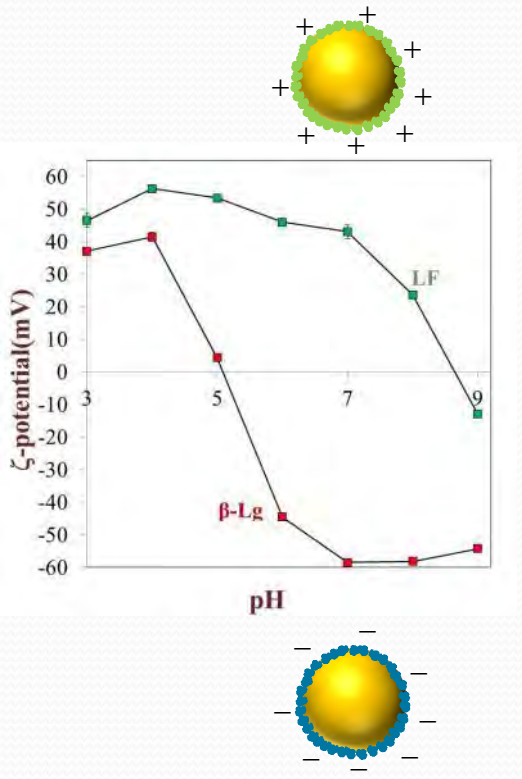
Structured Emulsions: Filled Hydrogel Particles



Designing Nanoemulsion Functionality:
Controlled Heteroaggregation

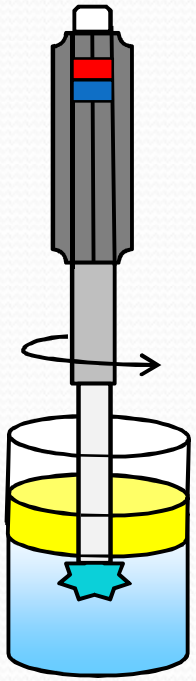


Controlled heteroaggregation of mixed lipid droplet systems – the structure formed depends on the ratio of the different kinds of particles



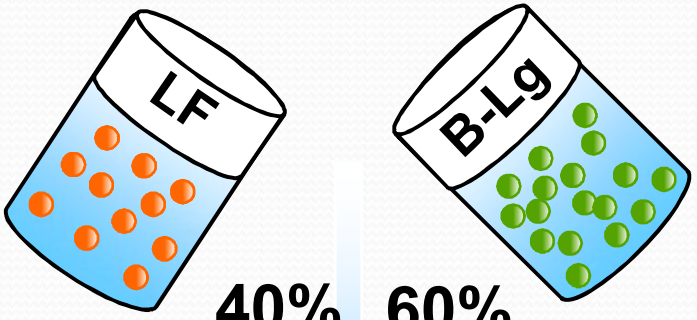
Designing Nanoemulsion Functionality:

Controlled Heteroaggregation



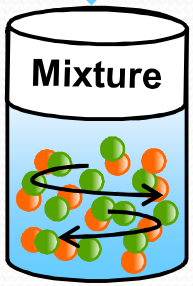
pH 7 No salt

9Kpa, 4 Passes

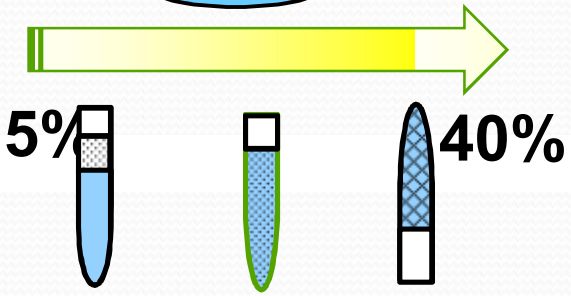


40% 60%

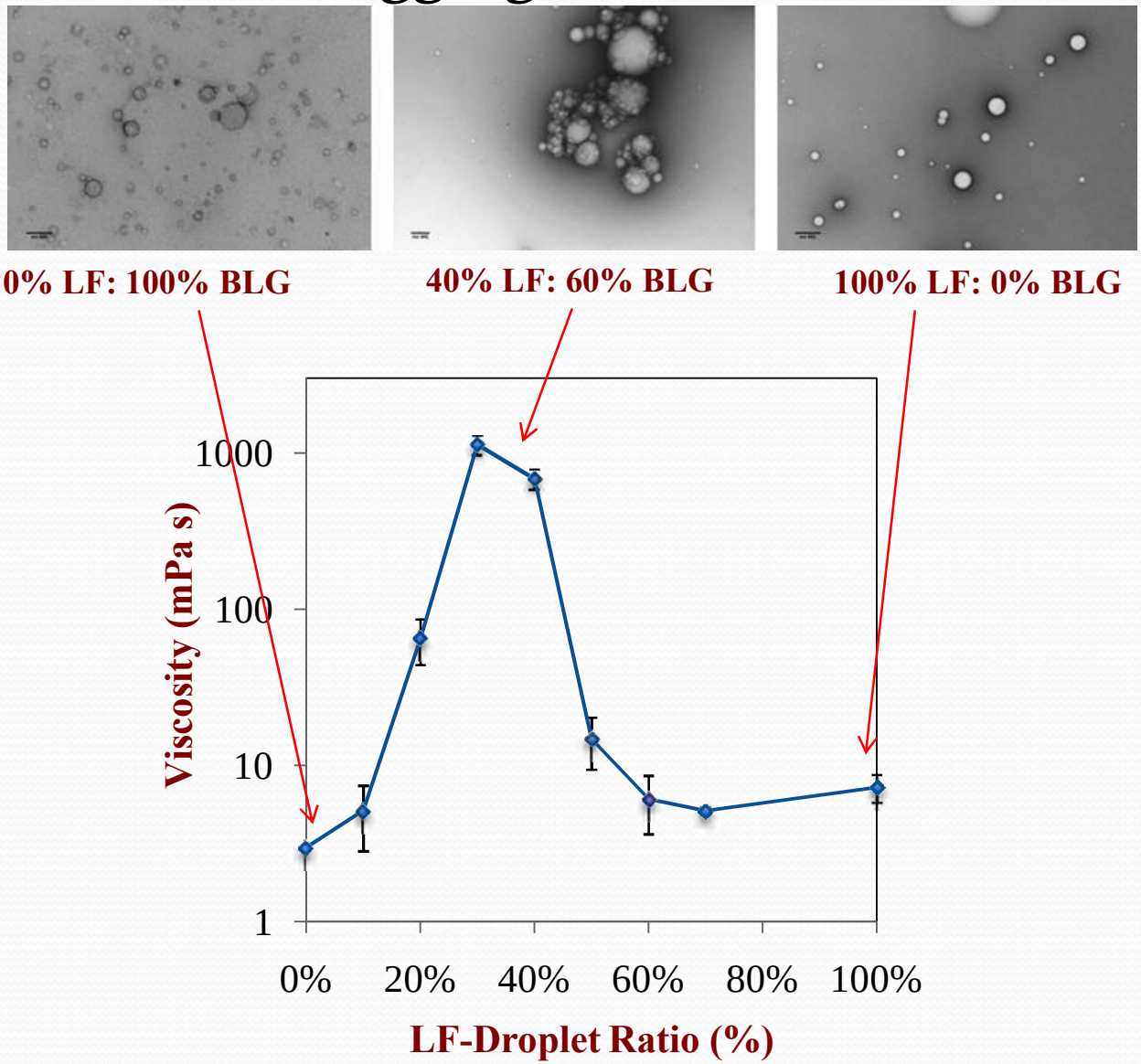
Stir for 10 min and stored over night



- Particle size & ζ-potential
- Rheology (viscosity & oscillation)
- Appearance Determination
- *In Vitro* Digestion

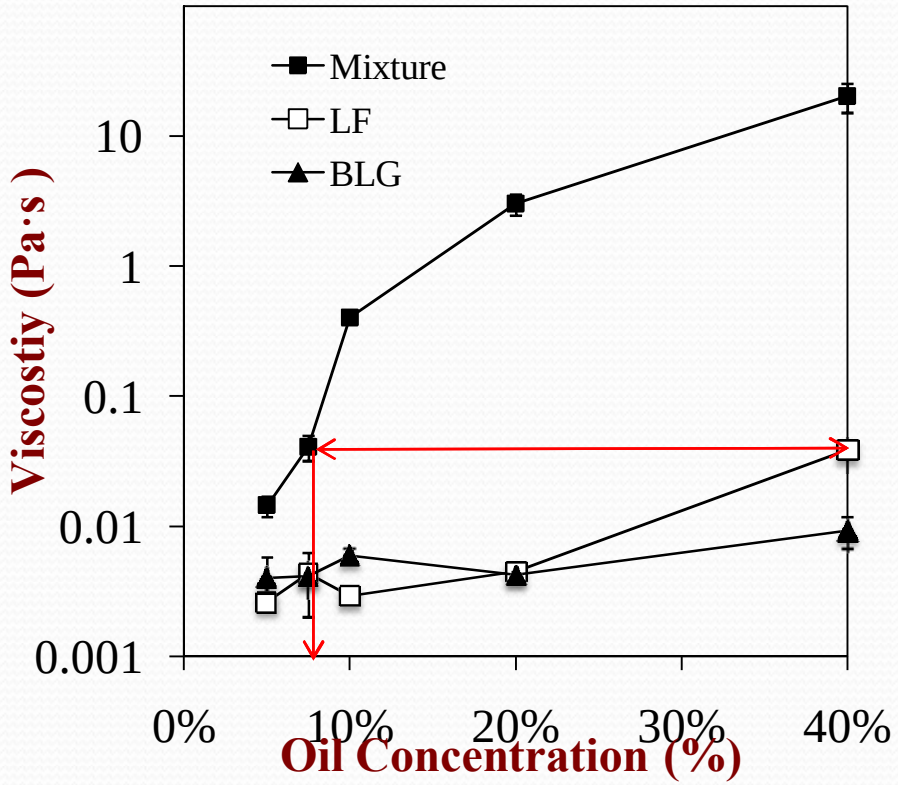


Designing Nanoemulsion Functionality:
Controlled Heteroaggregation



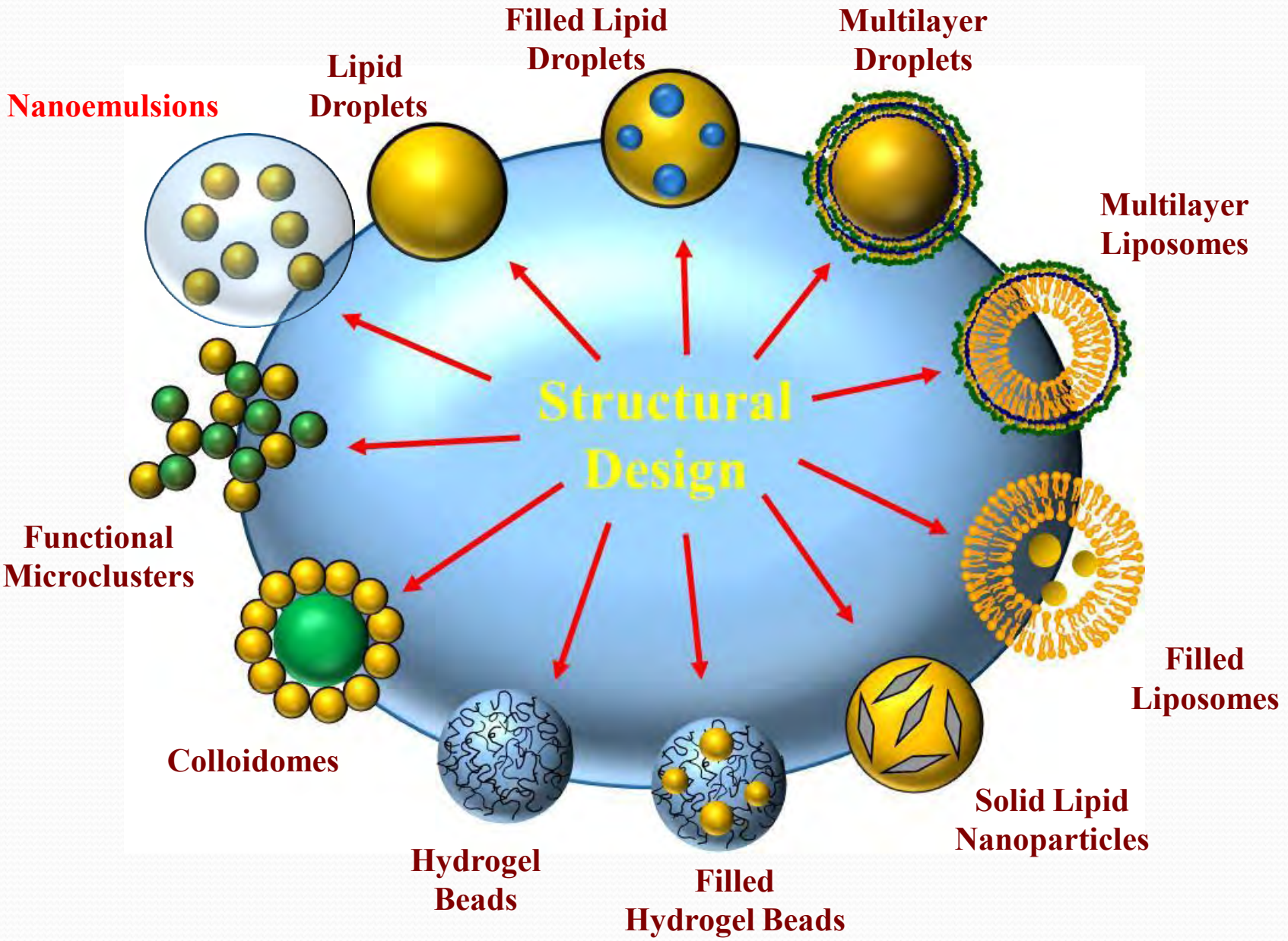
Viscosity Enhancement

Low fat mixture ≈ High fat single emulsion



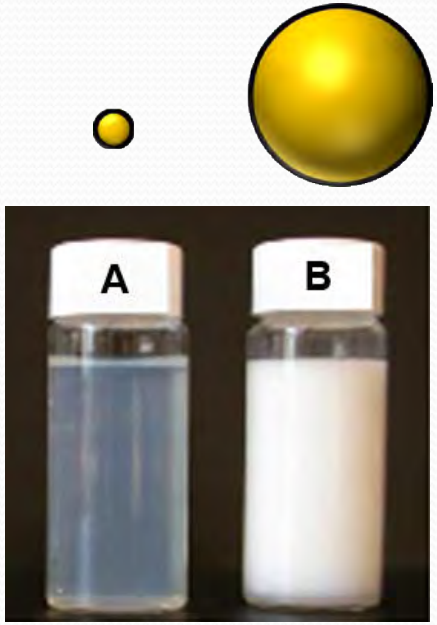
Viscosity of Different Fat Content Mixtures (LF40%: ϐ-Lg 60%), LF and ϐ-Lg Emulsions at Shear Rate (10 s^{-1})

Structured Emulsions: Filled Hydrogel Particles



Nanoemulsions

A nanoemulsion consists of two immiscible liquids (usually oil and water), with one liquid being dispersed as very small spherical droplets in the other liquid.



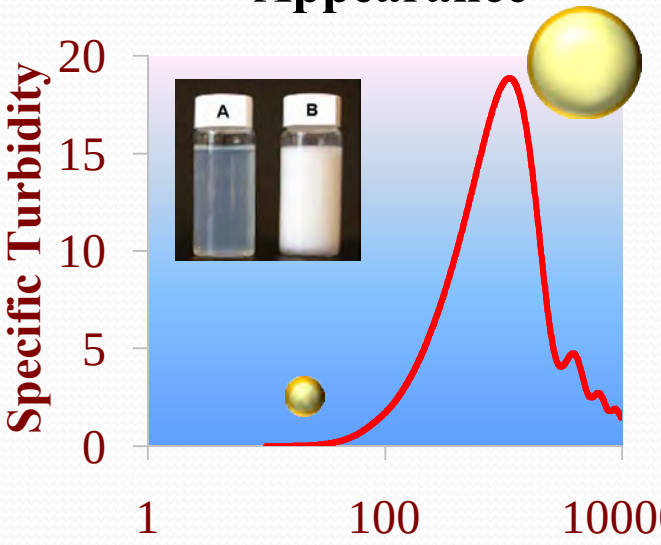
Nanoemulsion Emulsion

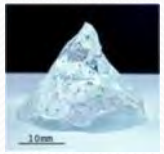
Characteristics:

- **Thermodynamically unstable**
- **Particle Diameter (d < 100 nm)**
- **Optically Transparent**
- **Intermediate Surfactant-to-Oil ratio (≈ 1:1)**
- **High Surface Area (30 m^2/g)**

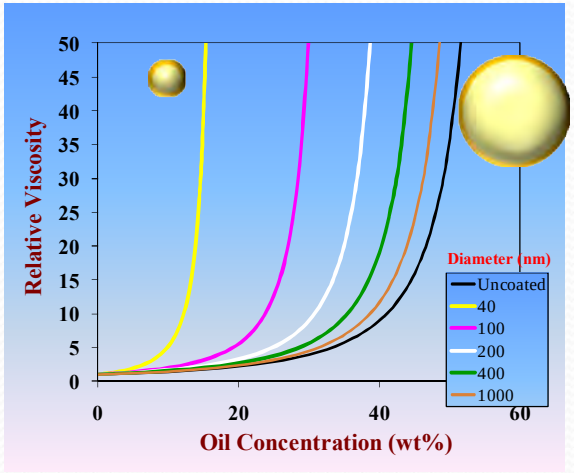
Nanoemulsions: Influence of Particle Size on Physicochemical Properties

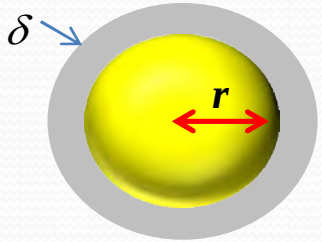
Appearance





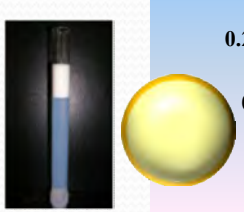
Texture

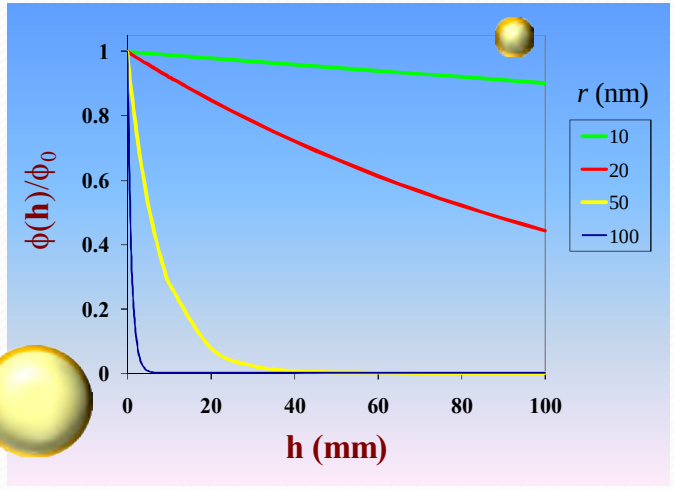




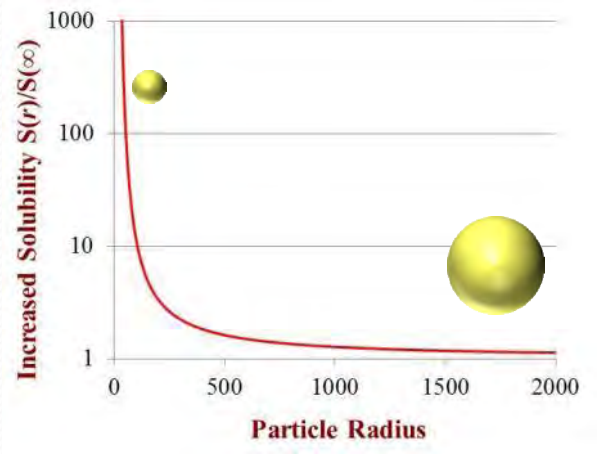
Shell makes large contribution

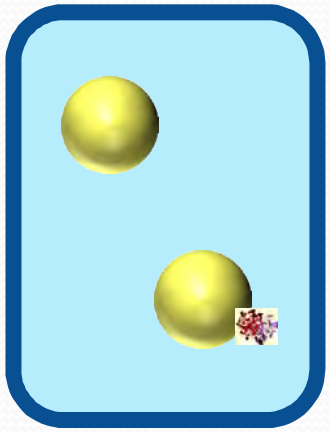
Stability



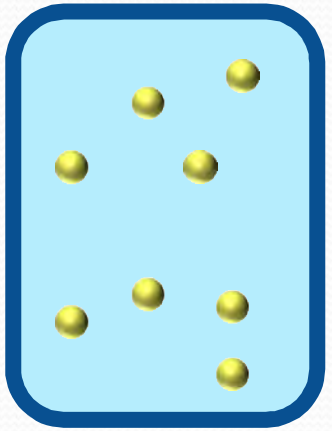


Nanoemulsions & Bioavailability:
Potential Influence of Particle Size on Biological Fate





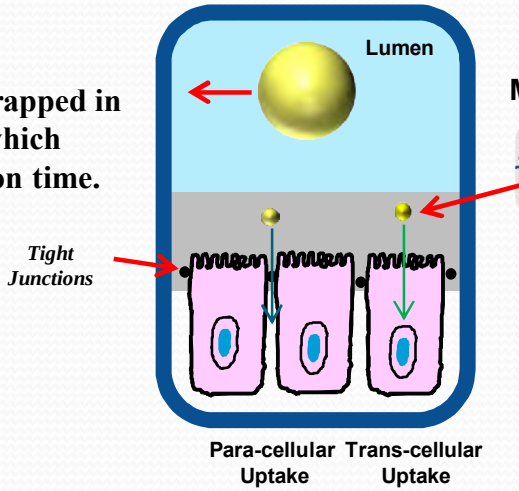
Larger particles
Smaller Surface Area



Smaller particles
Higher Surface Area

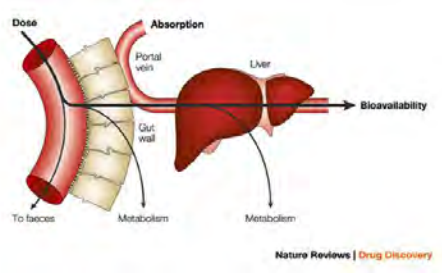
Van Eerdenbrugh (2010). MOLECULAR PHARMACEUTICS
VOL. 7, NO. 5, 1858ï 1870

Nanoparticles may be trapped in the mucous layer, which increases their retention time.

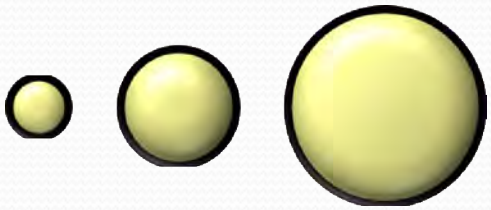


Large particles may be unable to enter the mucous layer.

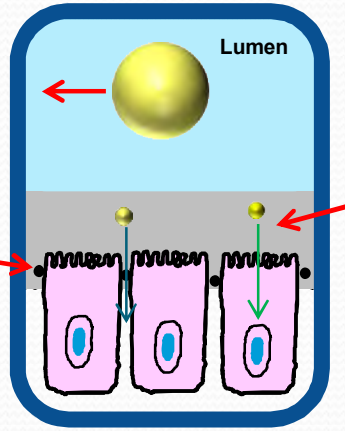
Nanoparticles may be digested & absorbed differently



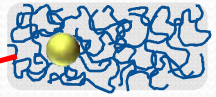
Nanoparticle Design



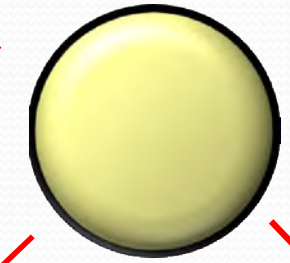
Digestible or
Non-digestible



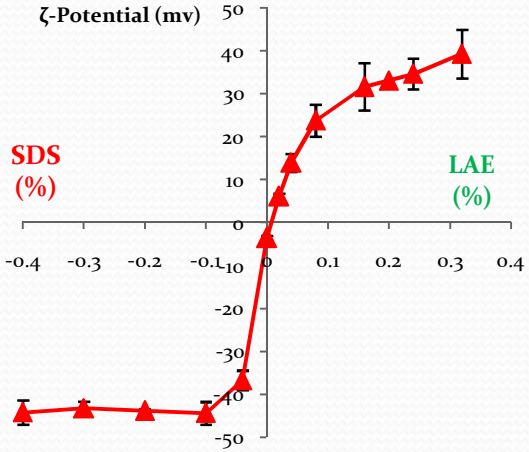
Particle Size



Nanoparticle



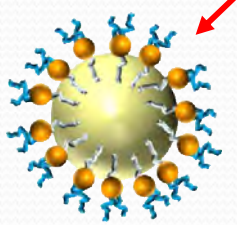
Composition

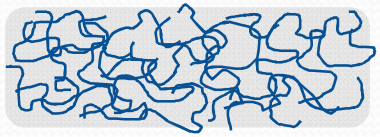


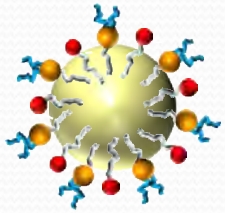
Specific Binding

Charge

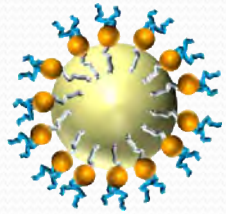
Specific Ligand



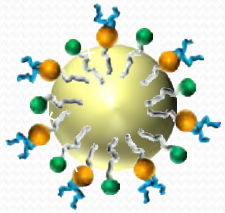




Negative



Neutral

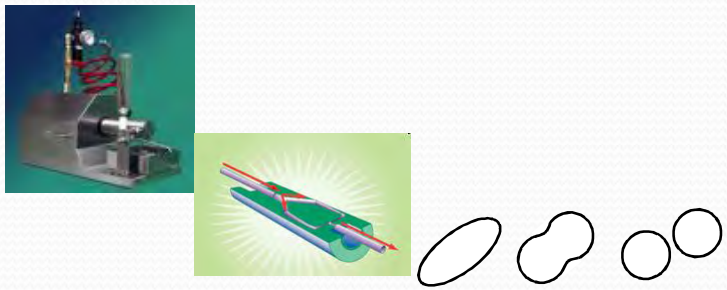


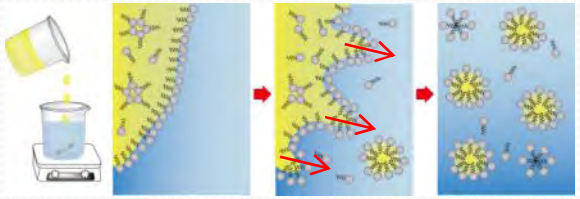
Positive

Food Nanoemulsions:

Fabrication Methods

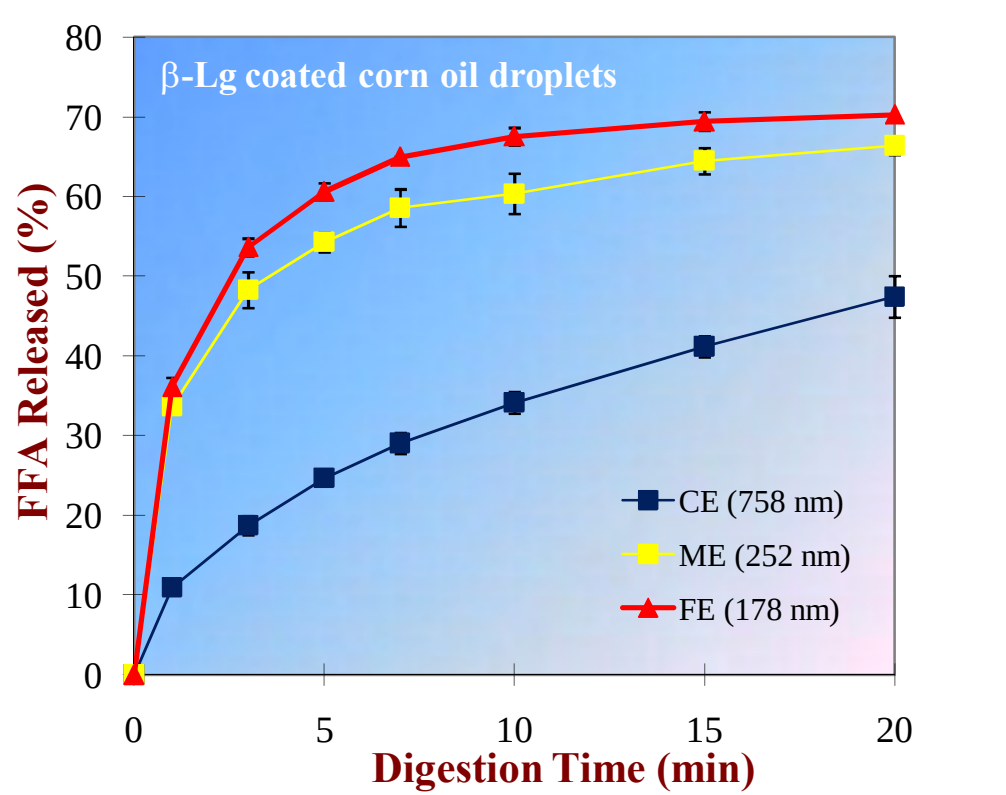
	High Intensity Methods	Low Intensity Methods
Principle	Break liquids into smaller parts using high intensity mechanical energy	Spontaneously form droplets due to changes in physicochemical properties of phases
Examples	Ultrasonics, HPVH, Microfluidizer	Spontaneous emulsification, phase inversion methods (PIT, PIC & EIP)

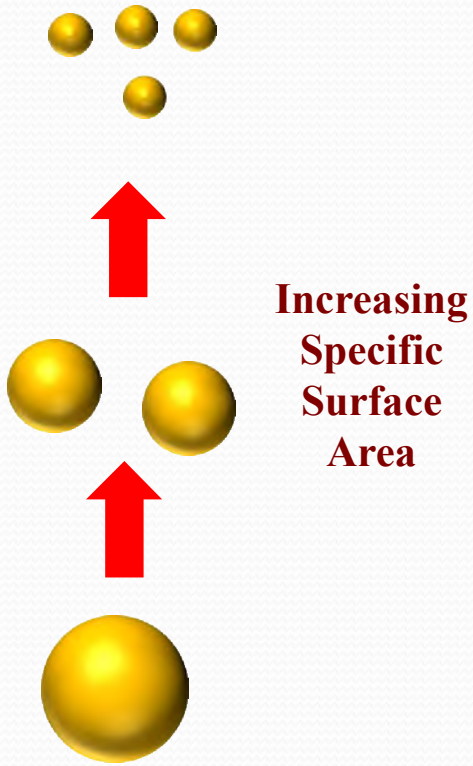




Nanoemulsions vs. Emulsions:

Influence of Droplet Size on Lipid Digestion

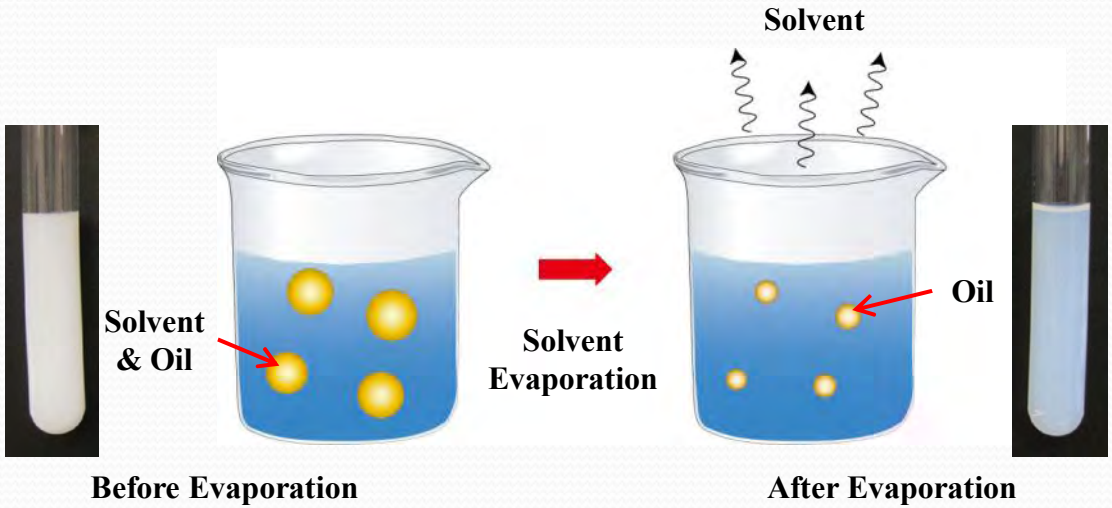




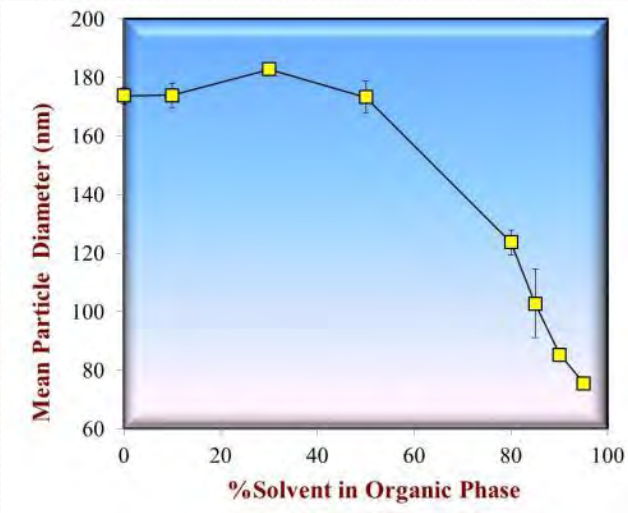
$k = 1 - 10$ mmol s^{-1} m^{-2}

In vitro digestion rate (per second) decreases as surface area of lipid exposed to aqueous phase increases (for similar interfacial character)

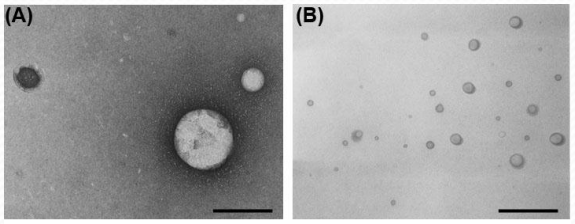
Nanoemulsion Formation: Solvent Removal Techniques



Corn oil-in-water emulsions (WPI)



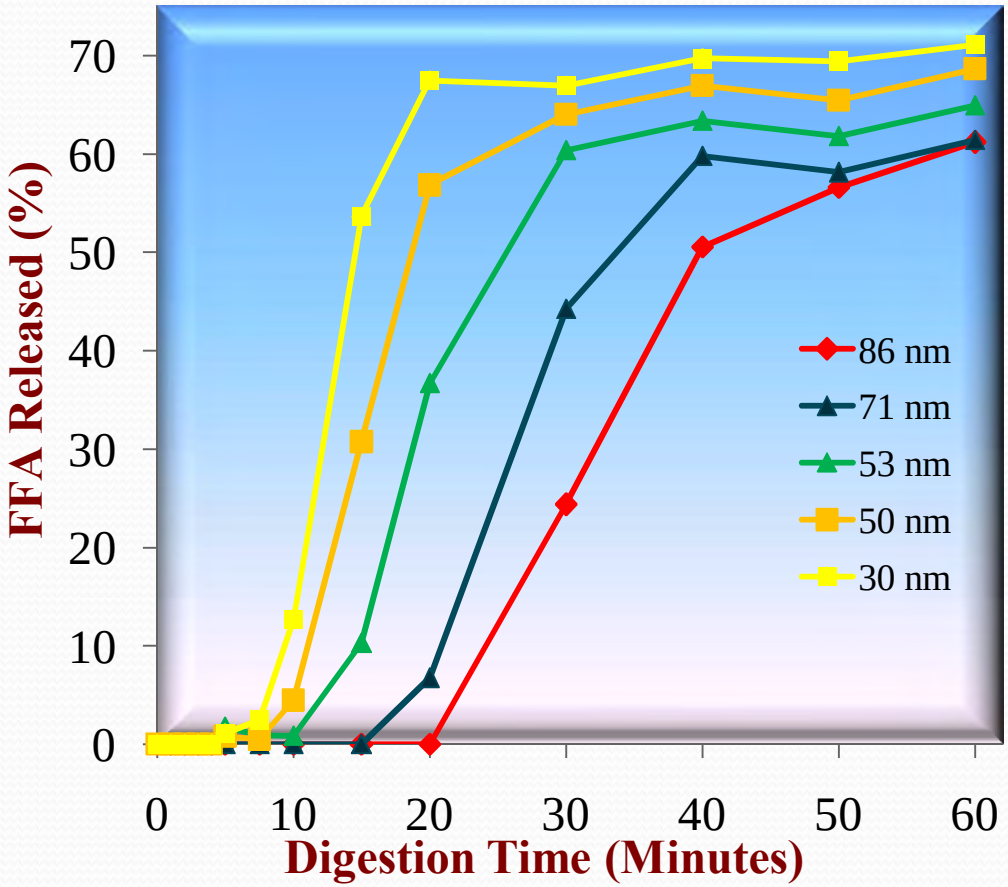
$$r = r_0 \left(\frac{V}{V_0} \right)^{1/3}$$



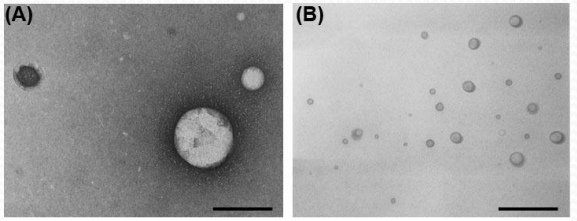
Before After

To reduce particle radius by ½th need to reduce volume by 1/8th

Nanoemulsion Digestibility: Influence of Particle Size & Free Surfactant



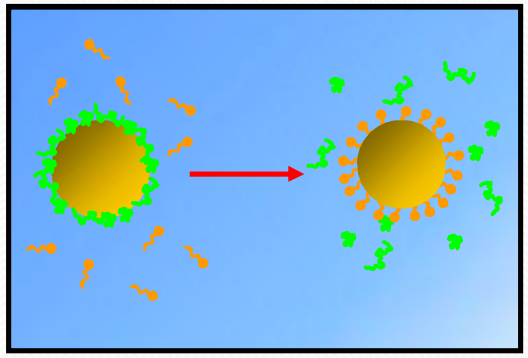
Variation in the amount of free and bound surfactant present



Before

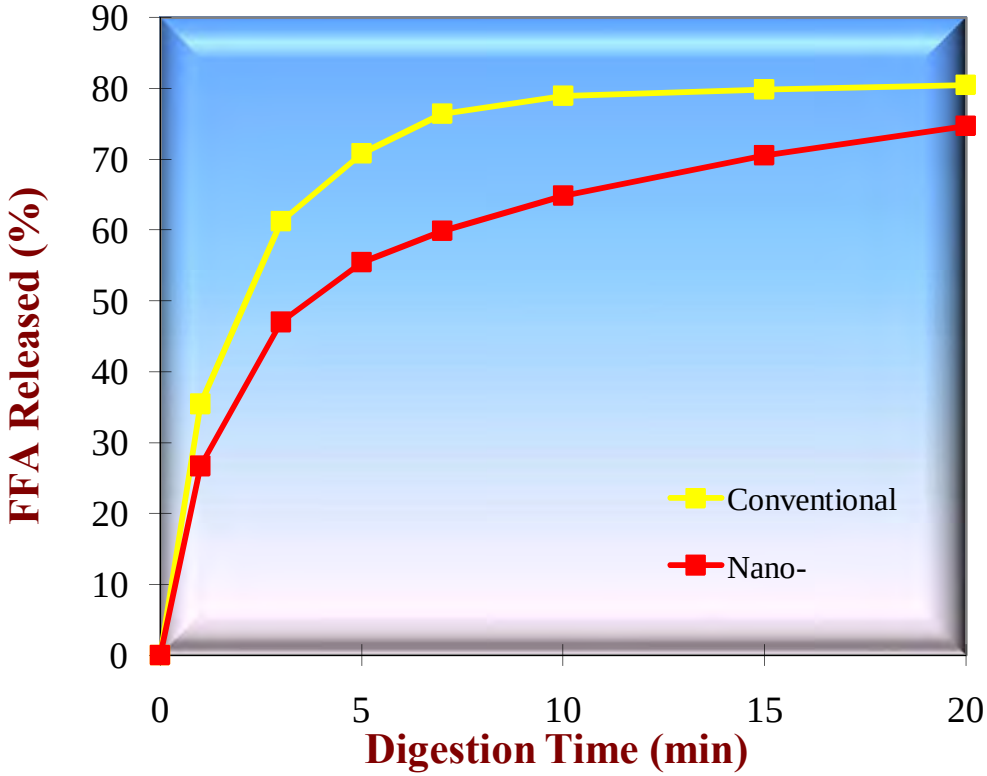
After

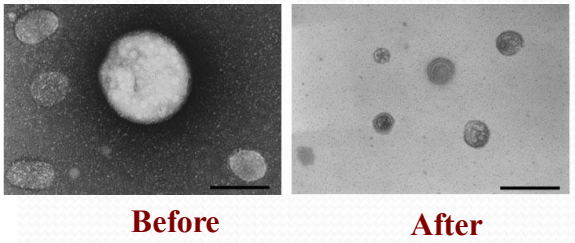
Competitive Adsorption & Displacement

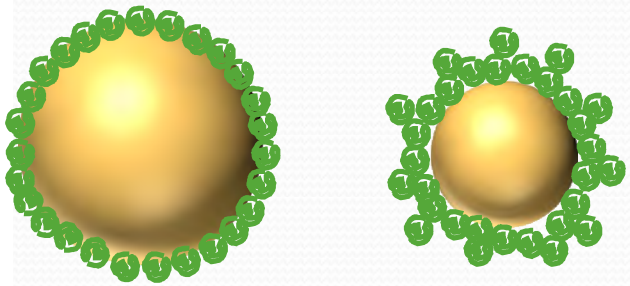


Tween 20 Stabilized Corn oil:Hexane

Nanoemulsion Digestibility: Influence of Particle Size & Interfacial Structure



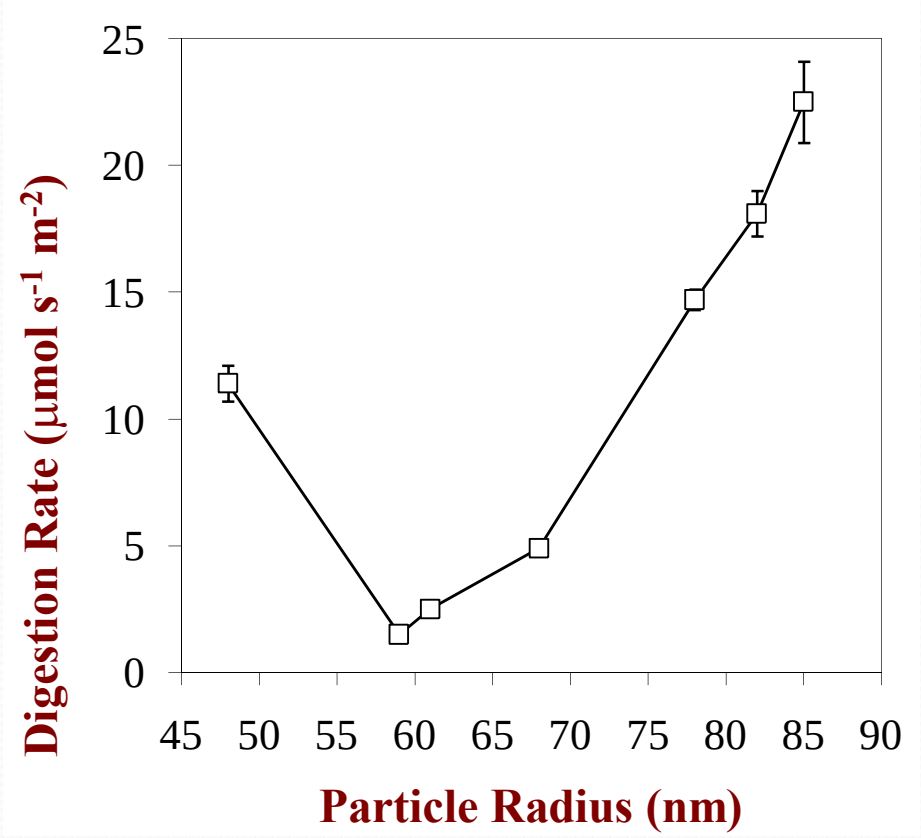


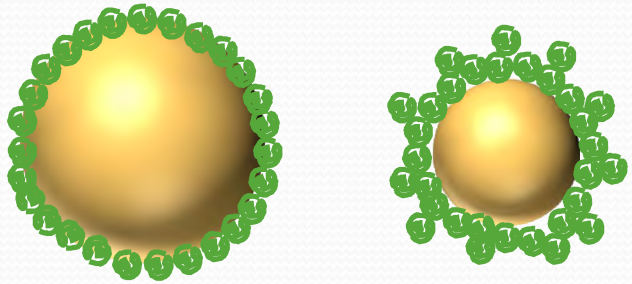


BLG-stabilized emulsions

- Interfacial structure plays an important role also

Nanoemulsion Digestibility: Influence of Particle Size & Interfacial Structure



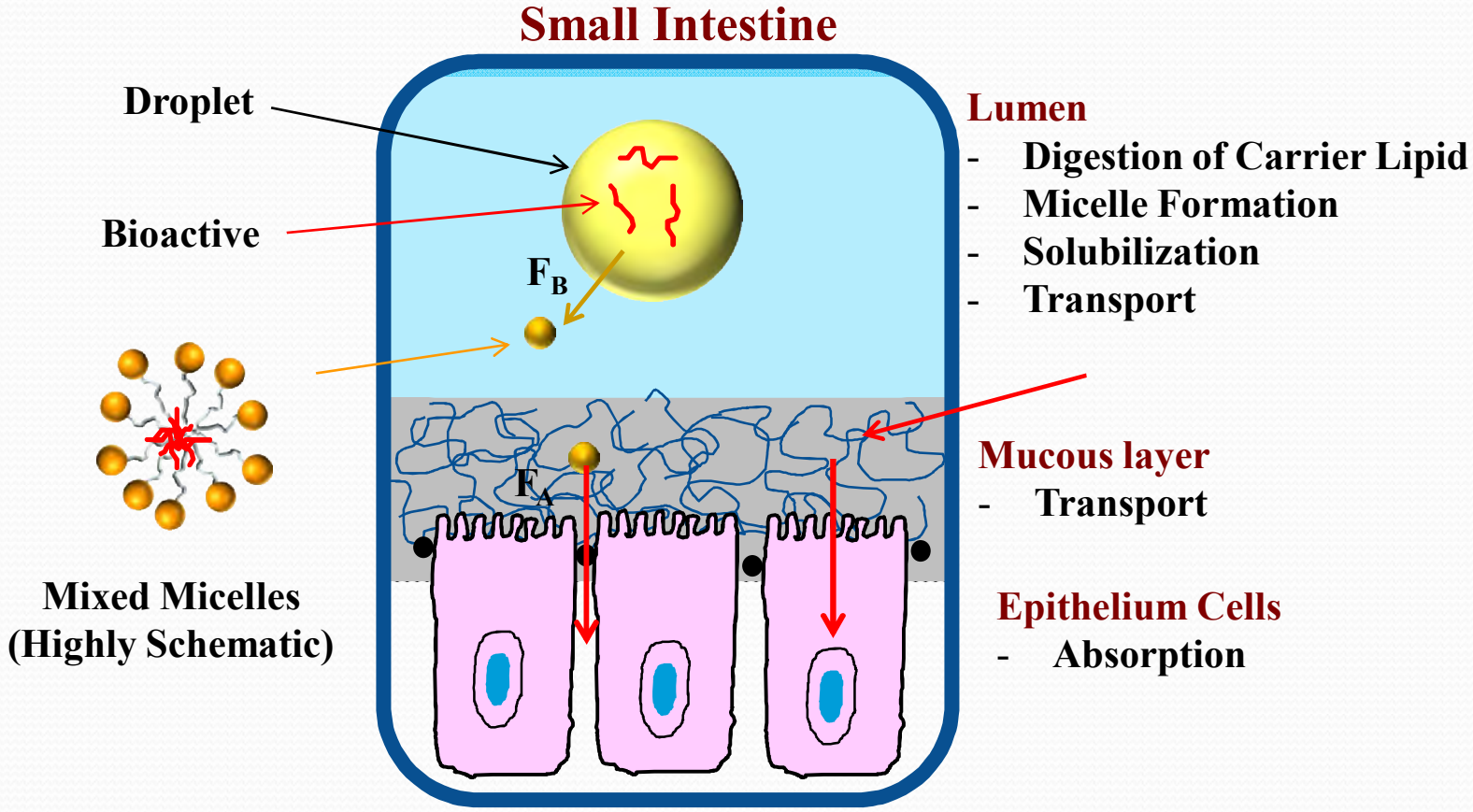


BLG-stabilized emulsions

Conclusion:

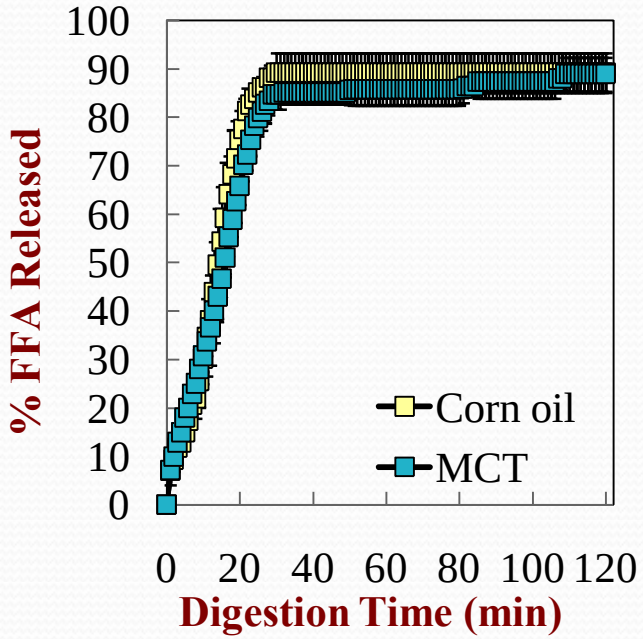
- Digestion depends on particle size, interfacial structure, and free surfactant

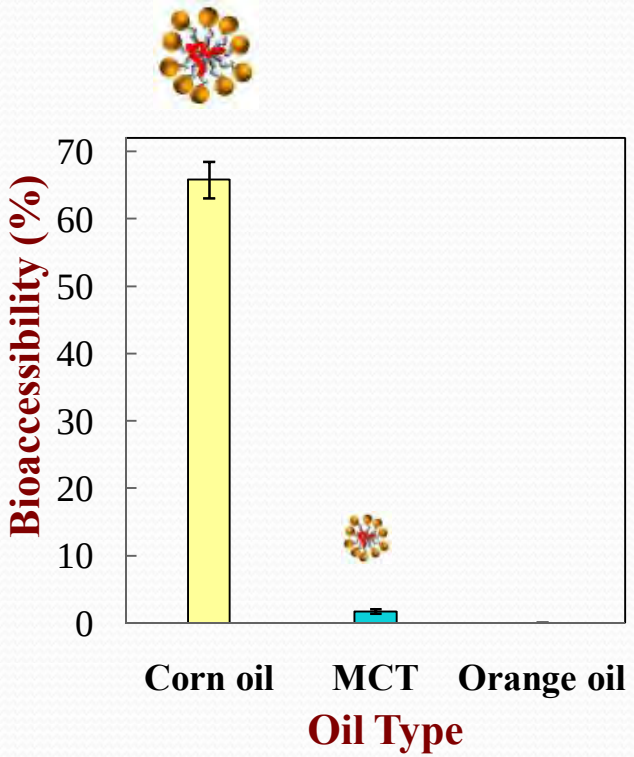
Biological Fate of Nanoemulsions:
Carrier Lipid Digestion and Solubilization

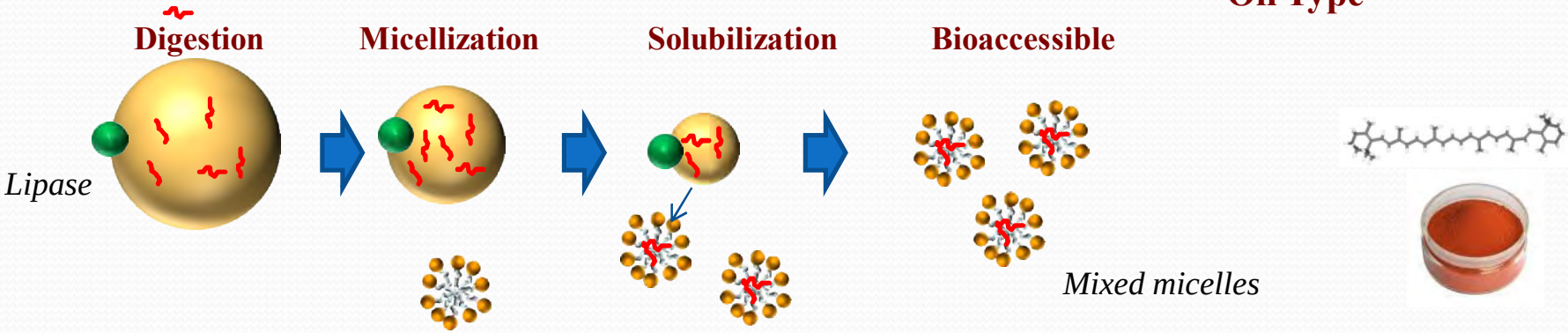


The bioavailability of encapsulated components often depends on the digestion of a lipid carrier oil, the formation of mixed micelles, and bioactive solubilization.

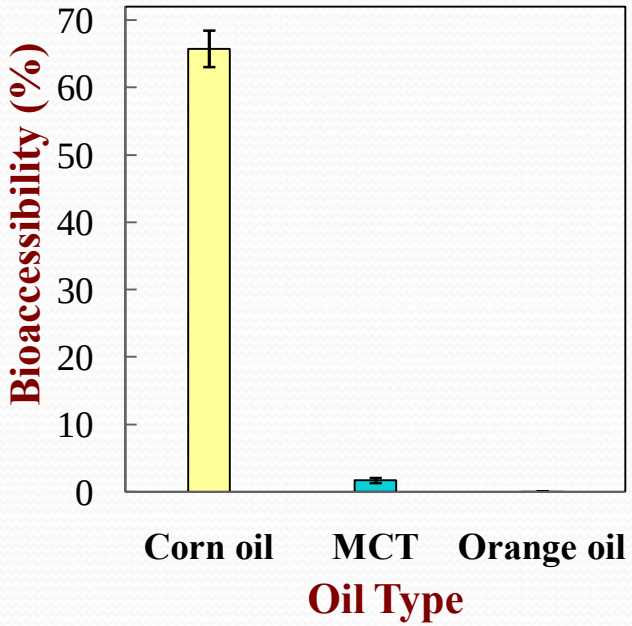
Encapsulation & Release of Nutraceuticals in Nanoemulsions: β-carotene



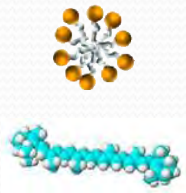




Encapsulation & Release of Nutraceuticals in Nanoemulsions: β-carotene bioavailability

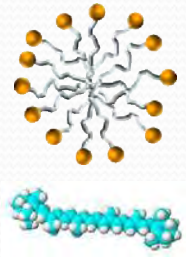


Small Mixed Micelles (MCT)



Too large to fit inside micelle

Larger Mixed Micelles (Corn Oil)

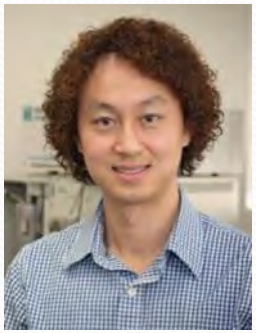


Fits in micelle

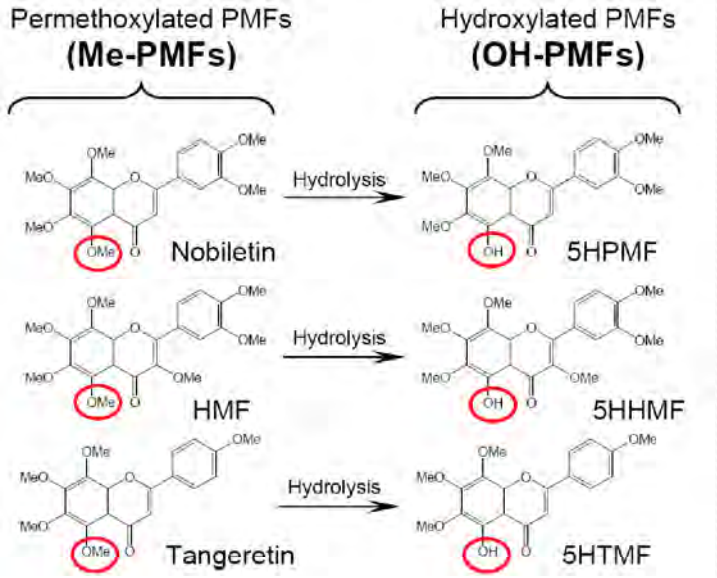
Conclusions:

- The bioaccessibility of bioactive components depends on size relative to micelles

Encapsulation & Release of Nutraceuticals in Nanoemulsions: Polymethoxyflavones (PMFs)



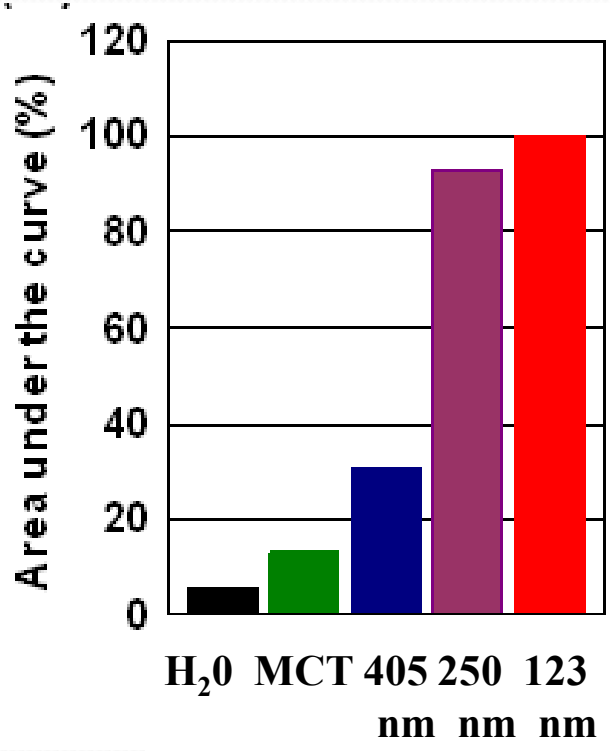
Hang Xiao



PMFs are a group of highly lipophilic crystalline flavoid compounds isolated from orange peel with potent anti-carcinogenic activity, but…

Å ***They are crystalline, have low water solubility and poor bioavailability***

Potential for Nanoemulsions to Improve Bioavailability: Polymethoxalated Flavones



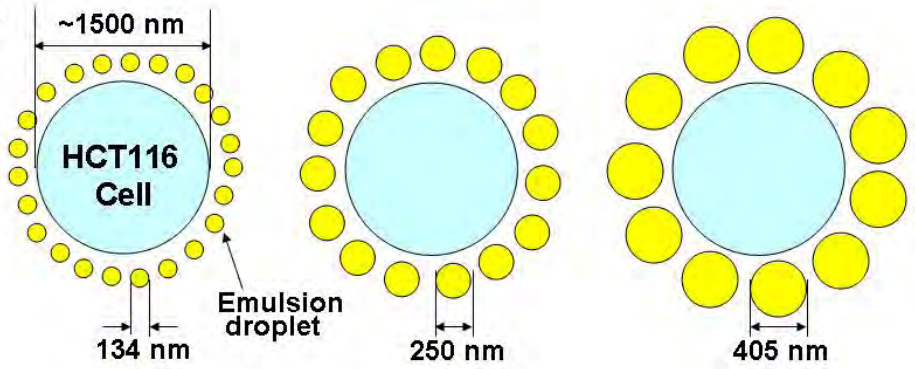
(A)

(10, 4) (6, 3) (5, 3)

(B)

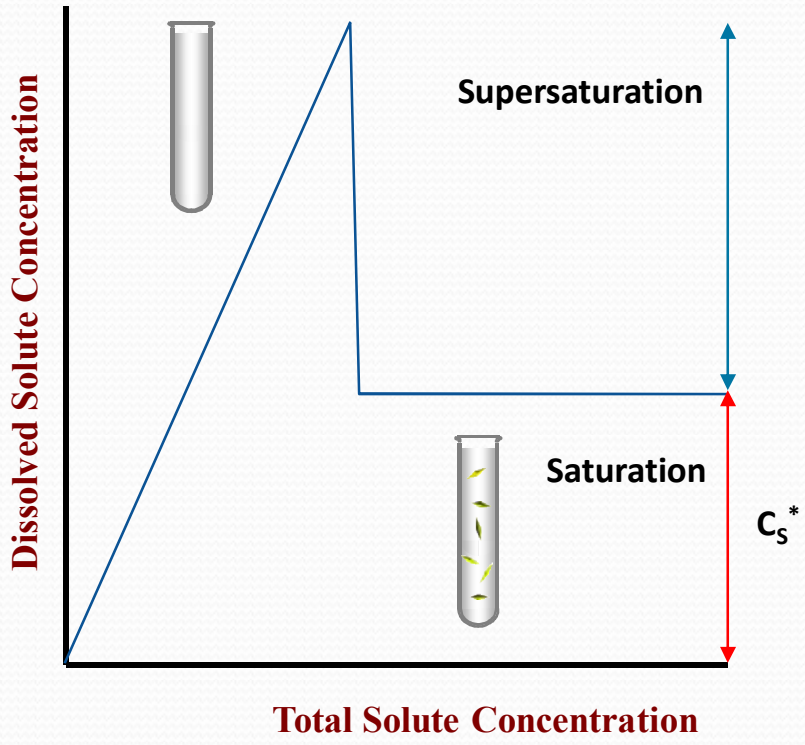
	Fresh emulsions		After 3 days	
(Pressure, cycle)	*d* (nm)	*Z* (mV)	*d* (nm)	*Z* (mV)
(10k, 4passes)	134	- 60.8	134	- 61.0
(6k, 3passes)	250	- 62.8	255	- 62.5
(5k, 3passes)	405	- 62.5	406	- 62.8

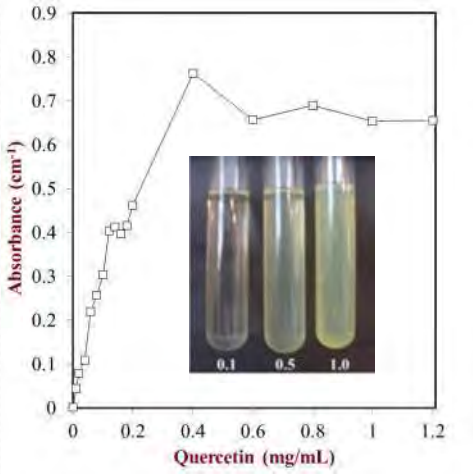
(C)



Encapsulation in Nanoemulsions:

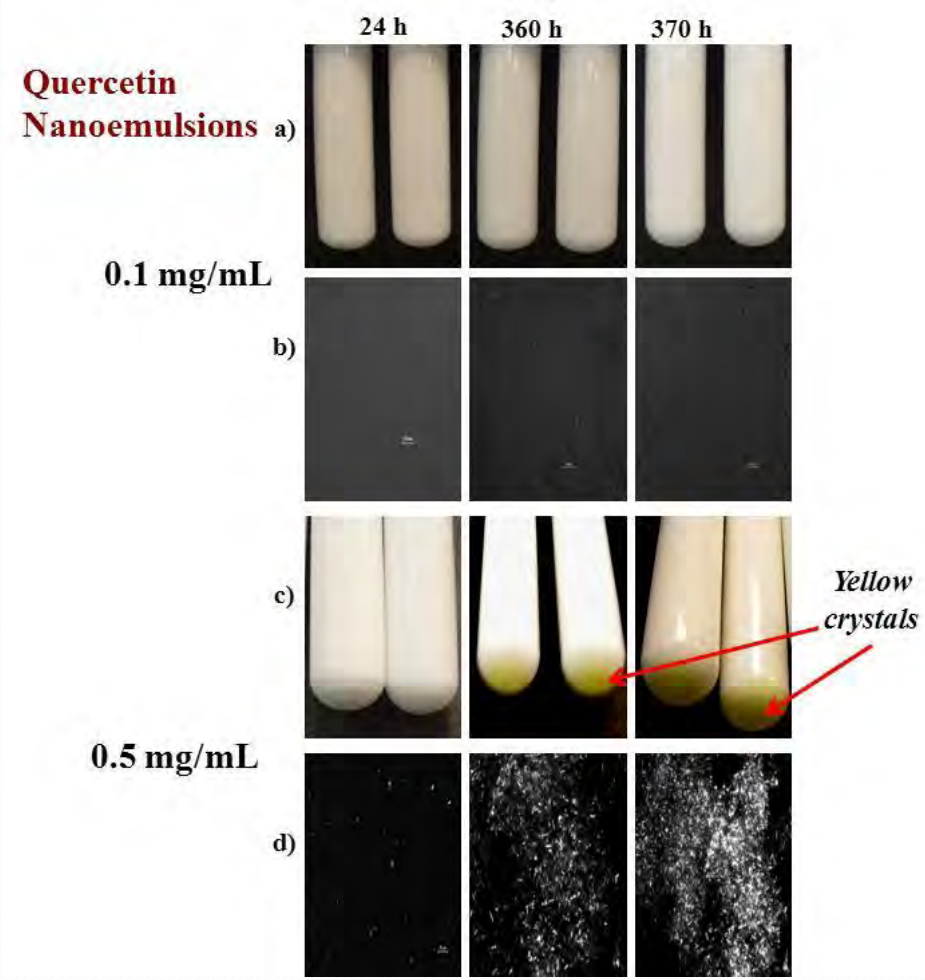
Problems with Crystallization





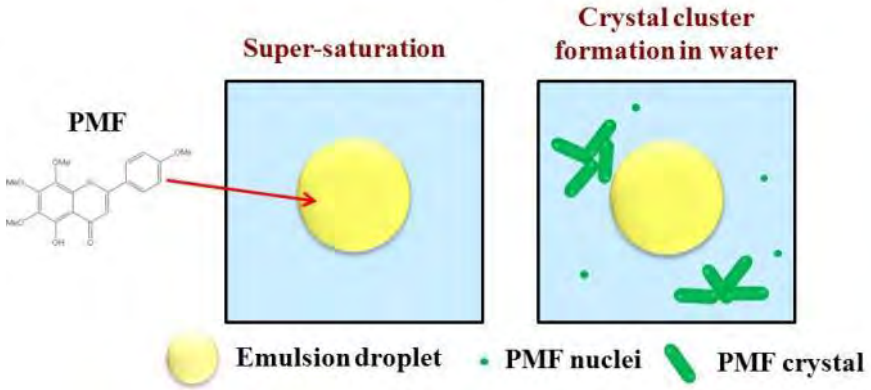
Many bioactive components have low oil and water solubility

Encapsulation in Nanoemulsions:
Problems with Crystallization

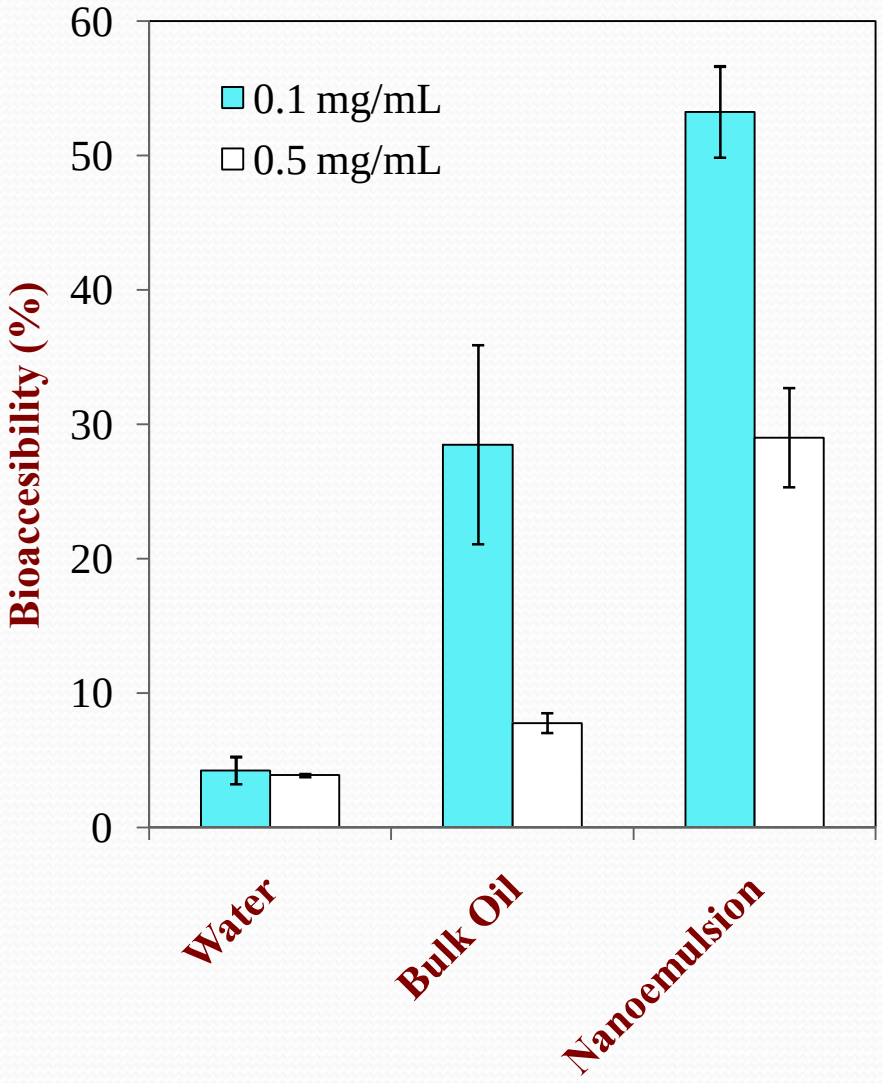


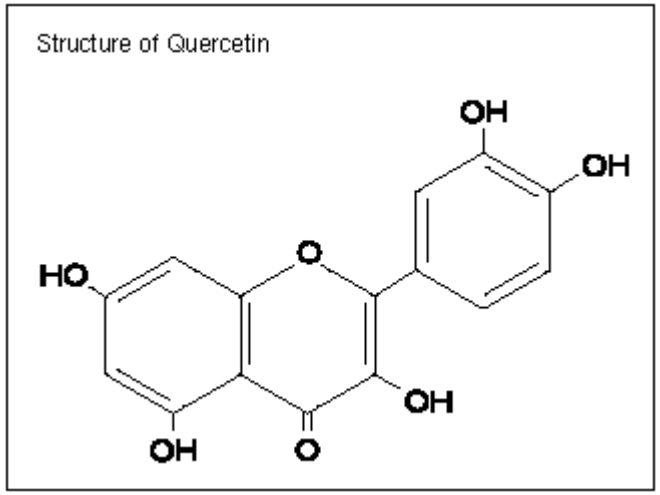
Potential Solutions:

- Use below saturation limits
- Induce super-saturation
- Keep crystals stable



Encapsulation in Nanoemulsions:
Problems with Crystallization





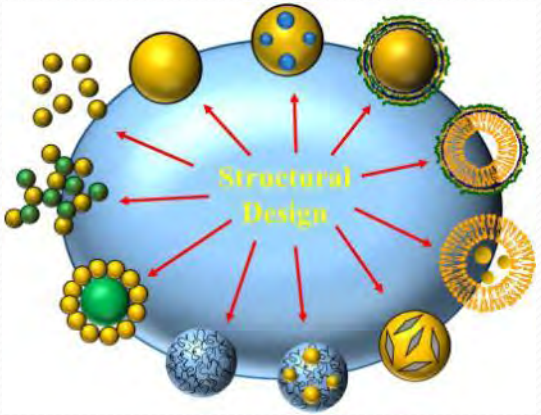
Quercetin bioaccessibility:

- Higher in emulsions
- Higher in soluble form

Conclusions

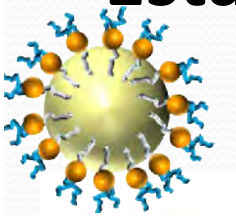
- **Structural design principles** can be used to create a wide variety of different emulsion-based delivery systems
- These delivery systems can be fabricated from food grade ingredients using simple processing operations.
- Delivery systems can be designed to improve functionality
  - *Control Digestibility*
  - *Control Release*
  - *Modulate Satiety*
  - *Create Reduced Fat Products*

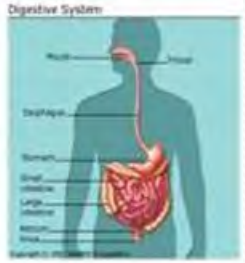
- The economics of formulation and production of structured emulsions needs to be assessed



Delivery System Design:

Establishing Performance Criteria





Matrix Compatibility
- Optical
- Rheological
- Stability
- Flavor

Processing
- Heating
- Cooling
- Drying
- Shearing

Storage
- Temperature
- Mechanical stress
- Light
- Oxygen
- Time

Consumption
- Appearance
- Texture
- Taste and Aroma
- Convenience

Ingestion
- Digestion
- Absorption
- Toxicity

Stable

Controlled Instability

DELIVERY SYSTEM CRITERIA:

ÅFabricated from food grade ingredients using economic processing operations.

ÅDesigned to function over wide range of conditions in food product and human body.

ÅSensory acceptance

Acknowledgements

Food Biopolymers and Colloids Research Group:

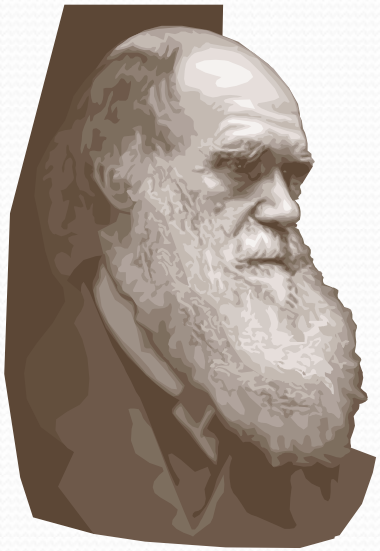
Faculty at UMass:

- **Eric Decker**
- **Hang Xiao**
- **Yeonhwa Park**
- **Lynne McLandsborough**
- **Julie Goddard**

USDA United States Department of Agriculture National Institute of Food and Agriculture

Food Development:

Evolution *vs.* Intelligent Design



versus

Evolution: **Most traditional foods evolved by small adaptations through history to become the familiar items we know today.**

Intelligent Design: **The modern food industry requires rapid innovation and implementation of new products – an intelligent design process should be favored.**